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Reactions Of Difunctional Esters With Benzyl 2-Amino-4,6-0-Benzylidene-2-Deoxy-D-Glucopyranosides

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REACTIONS OF DIFUNCTIONAL ESTERS WITH BENZYL 2-AMINO-4,6-O-BENZYLIDENE-2-DEOXY-D-GLUCOPYRANOSIDES

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By

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I would like to express my sincere gratitude to my wife, who has aided so many ways in the course of this research.

I also wish to take this opportunity to acknowledge the skillful direction of my research advisor, Paul H. Gross. His incisive intellect, comprehensive knowledge of the subject under consideration, and unstinting assistance in technical procedures are reflected throughout this dissertation.

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CHAPTER I

INTRODUCTION

This research is primarily interested in investigating the reactions of benzyl 2-amino-4,6-O-benzylidene-2-deoxy-D-glucopyranoside (I) with various esters. The advantage offered by this sugar is that an alcohol and an amine group are in close proximity, allowing studies of intermolecular vs. intramolecular reactions and observation on anchimeric assistance in intramolecular reactions.

There is little background material available on reactions of this type, due to the fact that the benzyl amino-glucopyranosides have only recently been resolved into their respective anomers by Gross and Zimmerman[7]. This was done by protecting the 2-amino group with the benzyloxycarbonyl group, a classical procedure in peptide chemistry. The resolved sugars with the 2-amino group free, that is Ia and Ib, became available only shortly before the commencement of this research when methods of removing the N-acyl group were reported by Gross and Jeanloz[8].

While the structural complexity of Ia and Ib makes these compounds rather inconvenient to synthesize as starting material for these investigative reactions, certain definite advantages are gained by their use. With these anomers, the sugar ring, containing the hydroxyl and amine

groups, is held in a gather rigid position. This provides that the two reactive groups are held in positions spatially fixed from each other, an aid in considering what happens during the reaction and also convenient for spectrally analysing the products. For example, it is this rigid spatial configuration which no doubt accounts for the pattern of amide IR-spectra band shifts observed between the two anomers. Secondly, as the benzylidenated benzyl glucosamines have two benzyl groups, the products readily crystallize. This greatly aids in the ease of working up the products of the reaction mixtures.

The reactions involved in this research are either those of a type which have long been used in carbohydrate chemistry, such as O-acetylations, O-mesylations, and debenzylidenations, or they are of types which have had very limited investigation in this field. The shortness of the bibliography is due to the fact that few analogous reactions could be found in the field of carbohydrate chemistry, rather than indicating that a literature survey was not made.

CHAPTER II

MONOFUNCTIONAL ADDITIONS OF DIFUNCTIONAL ESTERS

The reaction between the two anomers of benzyl 2-amino-4,6-O-benzylidene-2-deoxy-D-glucopyranoside (I) and various difunctional esters has been studied (Table 2). As compounds I have a single alcohol and a single amine group available as reaction sites, and these groups are on adjacent carbons of the sugar ring, it was felt that the nature of these reactions might provide insight into possible blocking groups for the 2 and 3 positions. The synthesis and separation of the anomers of benzyl 3-O-acetyl-4,6-O-benzylidene-2-benzyloxycarbonylamido-2-deoxy-D-glucopyranoside was first reported by Gross and Zimmerman.[7] Larger proportions of β-anomer can be obtained in the glycosidation step by the method of Rhoads and Gross[11]. This procedure essentially consists of hydrolysis of the natural product chitin, the protection of the amino function by the benzyloxycarbonyl group, the formation of the benzyl glycoside, the addition of first the 4,6-O-benzylidene group and then the 3-O-acetyl group, and the resolution of the completely substituted sugar by fractional crystallization. The subsequent hydrolytic removal of the 2 and 3 blocking groups was performed with strong alkali in a single step, this not having been reported before.

Amide derivatives have been made by reaction of I

with acyl chlorides, or the free acid in the presence of a carbodimide[8]. However, esters had not been employed for the purpose of N-acylation of I.

Analogous to similar compounds prepared by Meyer zu Reckendorf and Bonner[2], the formamide anomers (IIa and IIb) were produced using methyl formamide in a methanolic methoxide solution. The ethyl oxamide anomers (IIIa and IIIb) were prepared by the method of Drefahl, Hartmann, and Skurk[6] previously used for making amides of 1-hydroxyl, 2-amino cyclohexane with diethyl oxylate in ethanol.

The above methods failed completely in reacting more complicated difunctional esters with I. It was found that compound I could form amides with some other esters by using the ester itself as the solvent and employing elevated temperatures. These reactions are summarized in Table 2. It should be noted that the times and temperatures given in the experimental section are critical. For example, the conditions for the reaction of Ib and diethyl malonate to form Vb are 150°C for 4 hours. A reaction temperature 20 C° higher for 1 hour results in tars and no product, this also being the case for 150°C and 6 hours reaction time. A reaction temperature 25 C° lower resulted in no noticeable reaction after 12 hours. Using the "correct" conditions, the product often starts to crystallize directly from the reaction mixture.

The methyl esters are considerably more reactive

than the ethyl esters. For example, the reaction temperature for dimethyl malonate, in the preparation of IV, is 35 C^{o} lower and the reaction time 2 hours less than for the corresponding diethyl malonate in the preparation of V. Dimethyl succinate could be reacted with Ia to form VIa, whereas solutions of Ib and diethyl succinate resulted in tars before the corresponding amide was formed.

As the ester increases in size, the yields decrease, or are non-existent. This can be attributed to two effects. First, reactivity decreases with ester size; even though the methyl esters are the most reactive, reaction conditions have not been found which will yield the methyl adipate amide. Similarly, ethyl cinnamate does not undergo reaction. Secondly, the products of the reaction of I with bulky esters seem to be more soluble in non-polar solvents, especially when compared to the ester. Since excess ester and product are separated by precipitation of the product with petroleum ether, this can explain the decreasing yields with the larger esters, and is difficult to avoid as the larger esters have quite high boiling points. These high boiling points exclude the removal of the excess ester by distillation.

A remaining relationship of interest with these compounds lies in the competition between substitution of the ester and addition to a double bond. The first route gives the expected amide and the second results in a secondary amine. With fumaric esters, only the amides

(VIIa and VIIb) are produced, while with maleic esters (which differ only in cis-trans isomerism from fumaric) both the amide (VIIIb) and the secondary amine (IXb) are produced. This provides evidence that the stericly strained double bond of maleic esters is more reactive than the fumaric double bond. With ethyl acrylate only the secondary amine product (Xb) was found. This represents the extreme case in the competition between the two reaction routes.

In examining the correlation between the IR-spectra and the structures of the amides, little pattern can be found between the minor variations of the ester band. However, the amide bands show several interesting points, and are listed in Table 1.

Of the ten comparable pairs in Table 1, the amide I and amide II bands of the α-anomers are of lower wave number than the bands of the corresponding β-anomers. The average shift is 15 cm^{-1}. A number of compounds show amide I bands at higher than normal frequency. This is in accord with the observation that electron withdrawing groups raise the frequency of this band[1]. The three cases where this occurs are with the formamide (II), oxamide (III), and methoxycarbonyl amino groups (XXVI). Each of these groups would be expected to be more electron withdrawing than an alkyl group. From the above it would appear that if two 2-N amide substituted anomers of the same sugar were available, the α and β anomers could be determined by

TABLE 1

RELATIVE IR-SPECTRA AMIDE I AND AMIDE II SHIFTS BETWEEN α AND β ANOMERS OF BENZYL 2-AMIDO-2-DEOXY-D-GLUCOPYRANOSIDES

Compound	Amide Band (cm^{-1}) I	II	Compound	Amide Band (cm^{-1}) I	II
IIa	1650	1530	IIb	1670	1550
IIIa	1670	1540	IIIb	1690	1550
IVa	1620	1540	IVb	1650	1540
Va	1640	1540	Vb	1650	1540
VIa	1630	1520			
VIIa	1630	1530	VIIb	1650	1540
			Xb	1640	1510
XIVa*	1630	1530	XIVb*	1650	1540
XXa*	1630	1540	XXb*	1660	1540
XXVIa**	1670	1530	XXVIb**	1680	1530
XXXa**	1670	1520	XXXb**	1680	1530
***a	1630	1530	***b	1640	1540

*From Chapter III

**From Chapter IV

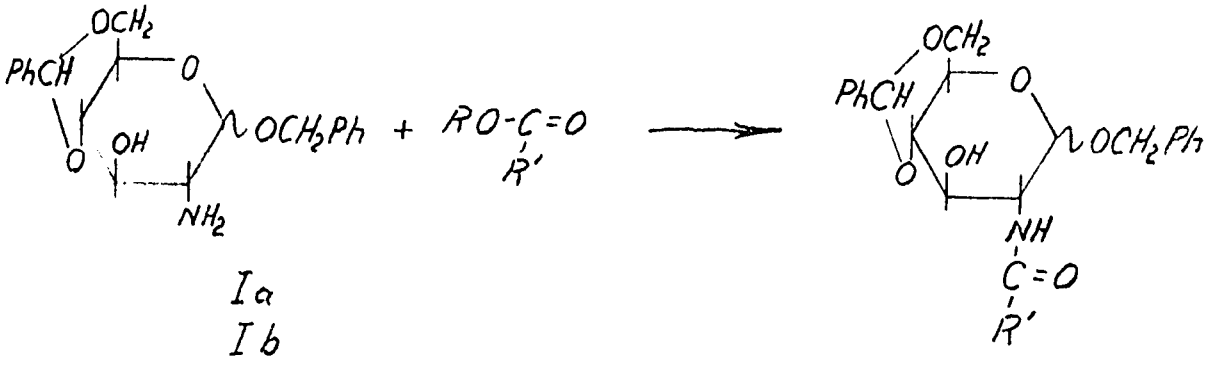
***Benzyl 2-acetamido-4,6-O-benzylidene-2-deoxy-D-glucopyranosides previously prepared by Gross and Jeanloz[8].

comparing the relative frequency of the amide bands.

This, however, is not entirely the case. The above compounds all have the 3 position unsubstituted. Nine pairs of anomers of 3 position substituted sugars of the above amides, which are reported in later chapters, have been made, and of these only three pairs show the expected relative shift.

The amide shift in α-β-anomers may prove to be useful in determining α and β linkages in disaccharides. This would have great advantages in simplicity, for at present the only way to make this distinction is by enzmatic cleavage, which is subject to uncertainties. However, to make this assignment, the 3 position next to the amide would need to be unsubstituted. The requirement of the 3 position being open should be of little problem, as this is the general case in disaccharides.

TABLE 2



Ia
Ib

IIa and IIb; R = Me, R' = H

IIIa and IIIb; R = Et, R' = -COOEt

IVa and IVb; R = Me, R' = $-CH_2COOMe$

Va and Vb; R = Et, R' = $-CH_2COOEt$

VIa; R = Me, R' = $-CH_2CH_2COOMe$

Me = $-CH_3$

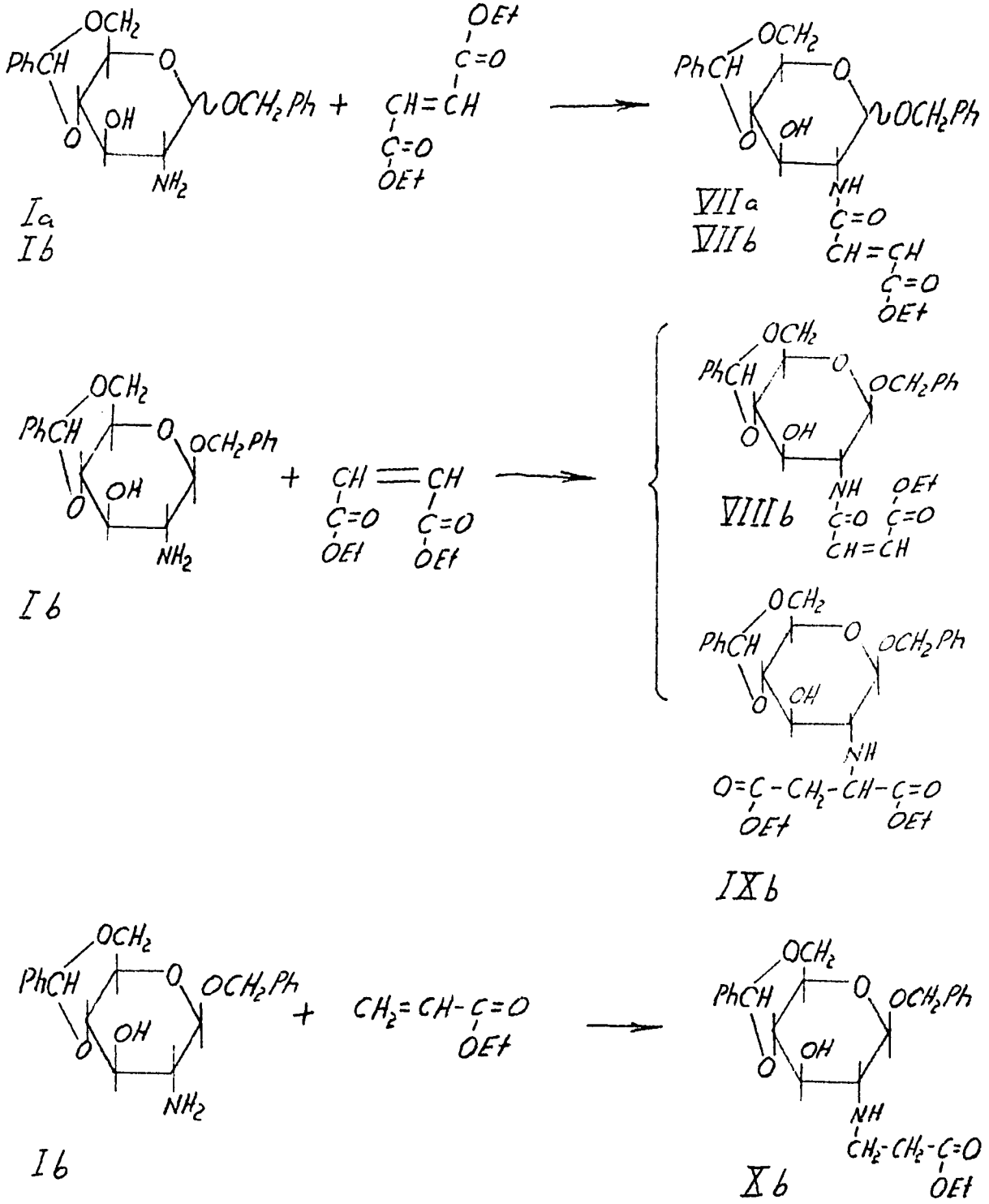
Et = $-CH_2CH_3$

Ph = $-C_6H_5$

a indicates α anomer

b indicates β anomer

TABLE 2 (CONTINUED)



CHAPTER III

REACTIONS OF BENZYL 2-ACYLAMIDO-2-DEOXY-D-GLUCOPYRANOSIDES

The anomers of II, III, and V (described in chapter I) were studied to determine if they would undergo normal acetylations, mesylations and debenzylidenations (Tables 3 and 4). The acetylations and mesylations would be expected to occur at the free 3 position. It soon became apparent that the anomers of III were unsuitable for such reactions, or their standard work up procedures. In each of the cases of debenzylidenation, acetylation, and mesylation, TLC and IR showed that the expected product was obtained. However, TLC showed that in each case minor products, which could not be moved from the starting point, were formed. This degradation could also be observed as the compounds moved across the TLC plate. Also, elemental analyses deviated from expected values. This could be interpreted as decarboxylation of the oxalate; however, if this were the case, the products would be formamides, that is, derivatives of compounds II. This is not the case as the corresponding derivatives of II move much faster on TLC than the degradation products of III. Therefore, a more plausible explanation is that these esters undergo hydrolysis to the oxalic acid derivatives, which under the TLC conditions used would be expected to have extremely low R_f values.

The anomers of II smoothly underwent acetylations (XIa, XIb, XVa, XVb) and debenzylidenations (XIIa, XIIb, XIVa, XIVb). The products are shown in Table 3. However, the mesylations gave two reaction products in each case. The IR-spectrum of one of the compounds showed that it was the expected 3-0-mesyl product of the starting material (XVIa, XVIb). The second compound (XVIIam XVIIb) was a sugar with an IR-spectrum showing no -OH, -NH, or amide bands, clearly a completely substituted product. With the exception of the usual alkane and aryl bands, the only prominent feature of the spectrum was a sharp band at 2140 cm^{-1}, indicating the isocyanide group. A search of the literature has revealed that recently, acid halides, in the presence of tertary amines, have been used to dehydrate mono-substituted formamides[13]. For example, benzenesulfonyl chloride and toluenesulfonyl chloride[9] in pyridine have been used for this purpose. Also, cyclohexyl isocyanide has been reported[12] with IR adsorption at 2138 cm^{-1}.

It is interesting to note that the most pronounced characteristics of isocyanides are: "an extremely distressing" odor, high chemical reactivity, and a semipolar formula for the functional group. None of the above seems to hold for XVIIa and XVIIb. The lack of smell can be readily attributed to the relatively high molecular weights and

high melting points. Compounds XVIIa and XVIIb are relatively unreactive in that they can be recrystallized from isopropanol, and that they show no sign of decomposition on relatively unactivated TLC plates using chloroform/methanol as the solvent. This, however, is not the first case of a highly reactive functional group becoming more stable on introduction into the sugar. The sugar epimines, previously prepared in this laboratory[11], show a similar lack of reactivity. The last point to note is that the isocyanide group does not seem to be extremely polar. With all other factors being equal, TLC R_f values are indices of the polarity of the compound. In these cases, the two products formed are identical except for XVI containing a formamide group, and XVII containing an isocyanide group. With both anomers, XVII moves much faster than XVI, which indicates less polarity for XVII. The use of methane sulfonyl chloride for isocyanide synthesis has not previously been reported, nor has the introduction of an isocyanide group into a sugar.

The anomers of V also smoothly under went acylations (XVIIIa, XVIIIb, XXIa, XXIb), mesylations (XXIIa, XXIIb), and debenzylidenations (XIXa, XIXb, XXa, XXb) with the ester group remaining intact in all reactions, as shown in Table 4. This series of compounds was studied due to the possibility of reaction (such as C-acylation) with the malonate group,

which has extremely labile C-H bonds as a result of the inductive effect of the two adjacent carbonyl groups. It was found that the reagents used affected only the sugar ring, and not the malonate. For example with acetylations and mesylations only the free hydroxyl groups were substituted. This could be shown by IR (the -OH bands dissappeared) by TLC (the relative R_f values of starting material and product are dependent on the number of unsubstituted -OH positions), and by elemental analysis (which would have shown excessive values for oxygen and sulfur respectively, had additional acylation or sulfonylation occured on the malonyl group). The results of the debenzylidenations could be verified on similar grounds. However, the malonate group can be modified without affecting the rest of the molecule. On treatment with sodium methoxide, a sodium salt of compound Vb is formed (XXIIb). Its IR spectrum shows all the functional groups of Vb remaining, and acidification of XXIIb yields the starting material, Vb. Therefore, XXIIb is the C-Na malonate salt. This is surprising when contrasted to diethyl malonate, which when subjected to analogous reaction conditions does hydrolize to form the half ester salt of the acid[3]. The different results with Vb may be due to the amide group replacing one of the ester groups, or may be due to an anchimeric effect of the 3-hydroxyl group.

TABLE 3

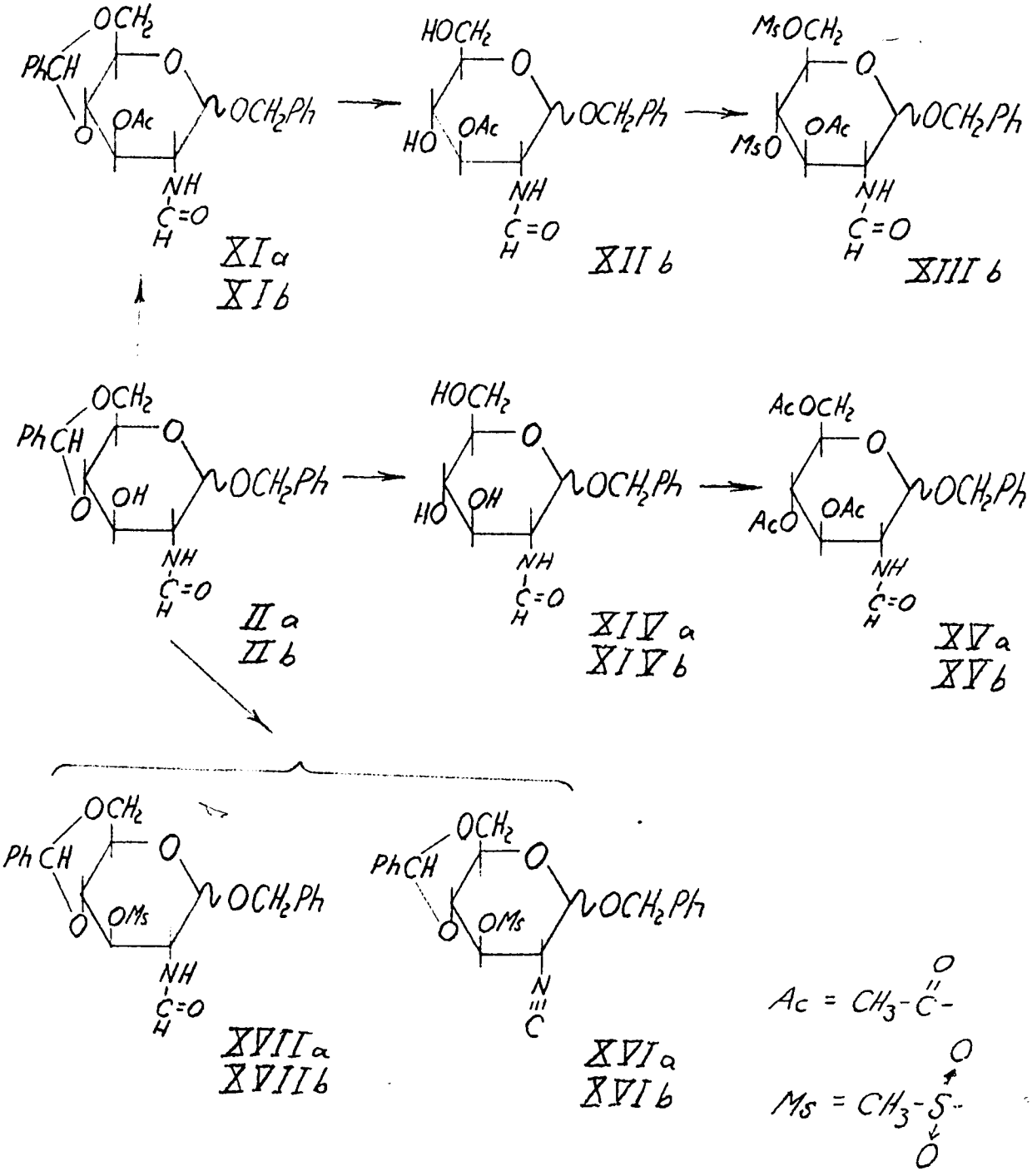

XIa
XIb
XIIb
XIIIb
IIa
IIb
XIVa
XIVb
XVa
XVb
XVIIa
XVIIb
XVIa
XVIb
Ac = CH3-C-
Ms = CH3-S-

TABLE 4

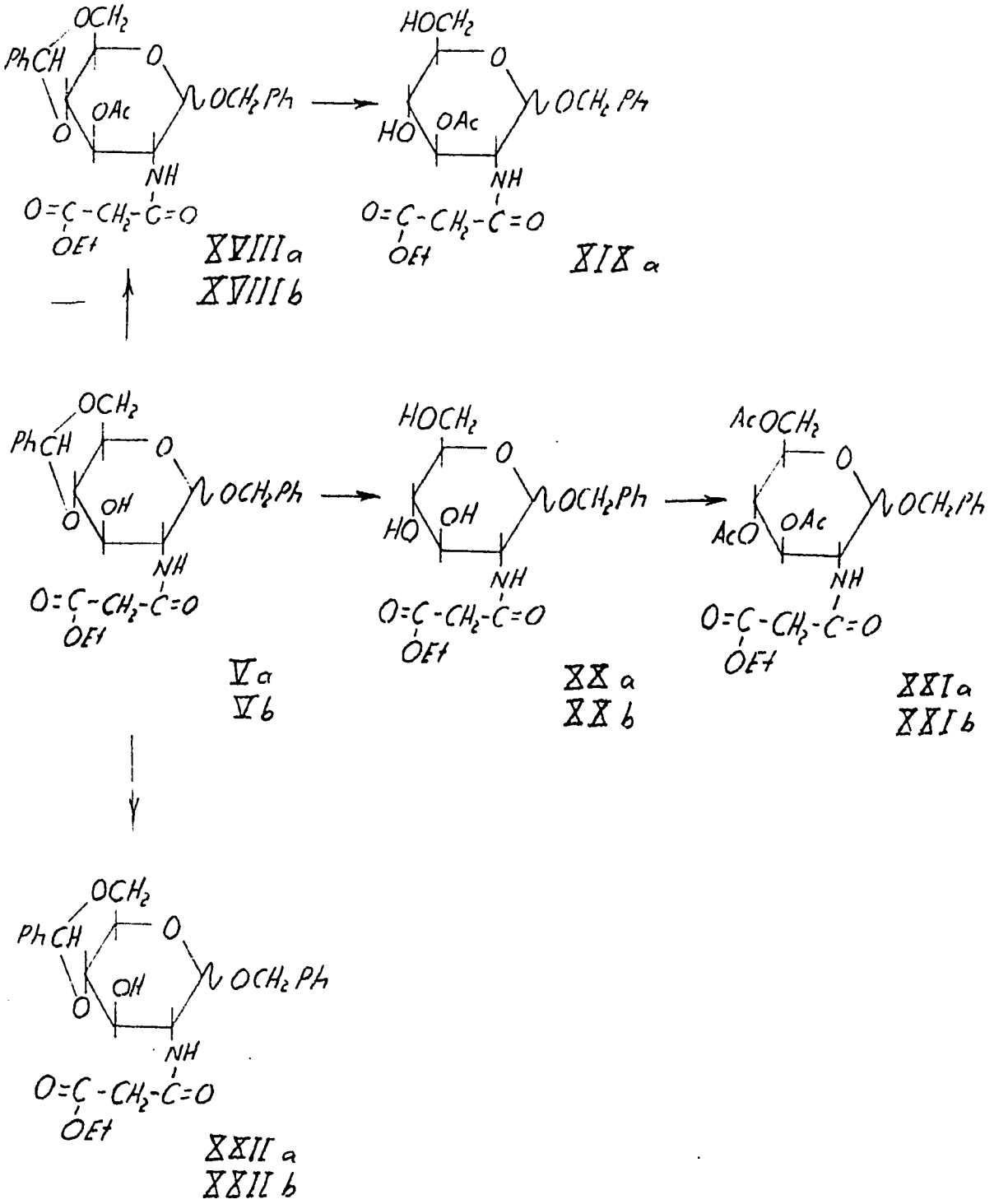
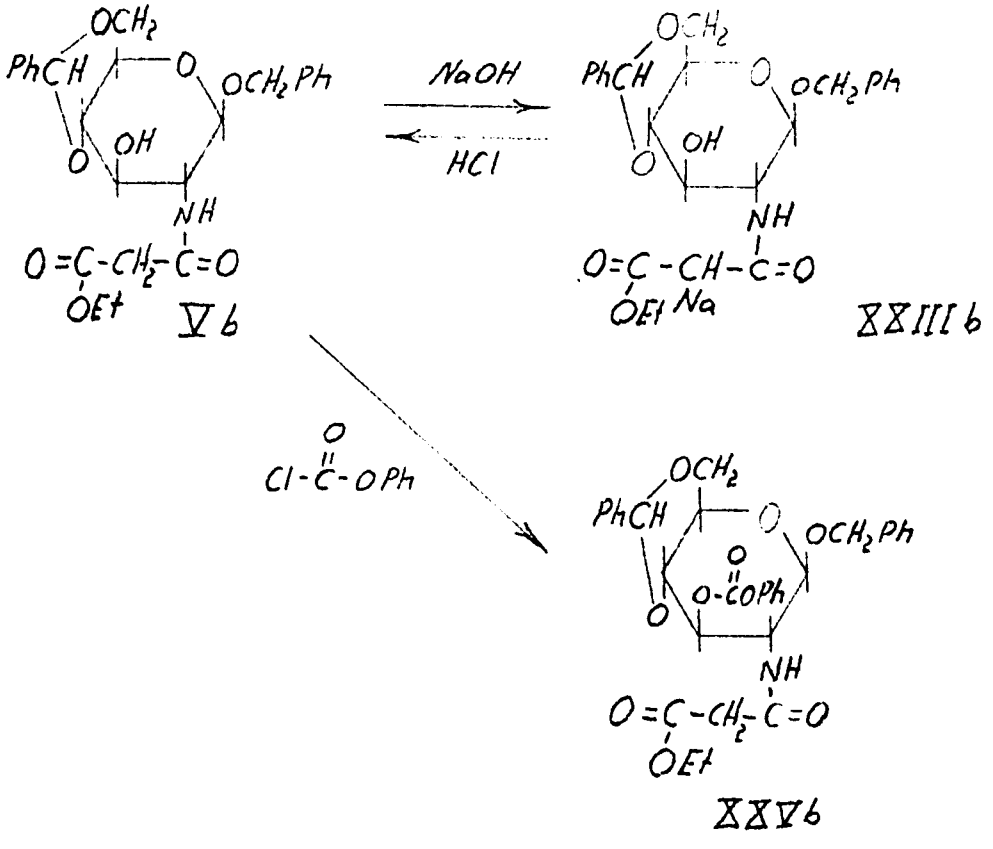

OCH2
PhCH
O
OAc
OCH2Ph
NH
O=C-CH2-C=O
OEt
XVIIIa
XVIIIb
HOCH2
HO
XIXa
V
Va
Vb
OH
XXa
XXb
AcOCH2
AcO
XXIa
XXIb
XXII
XXIIa
XXIIb

TABLE 4 (CONTINUED)



CHAPTER IV

DIALKYL CARBONATE REACTIONS

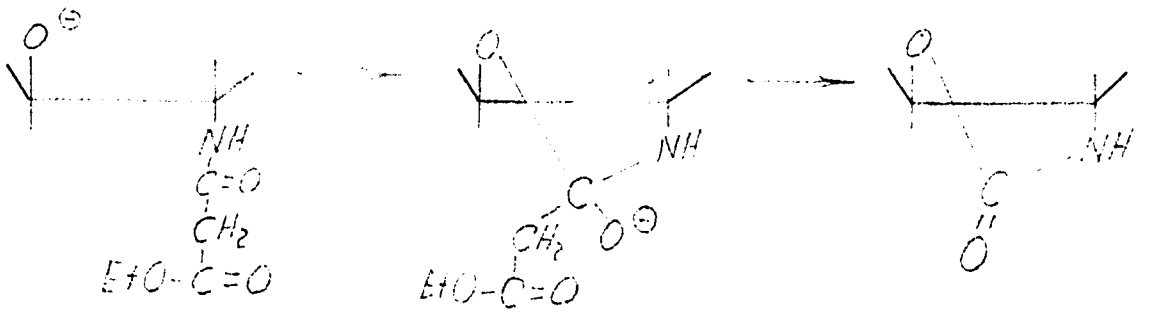
The reaction between benzyl 2-amino-4,6-O-benzylidene-2-deoxy-D-glucopyranoside (I) and dialkyl carbonates under basic conditions was shown to yield several products (Table 5). The ratio of yields of these products is temperature dependent. Dialkyl carbonate (diethyl or dimethyl) was the solvent, with the base, potassium tert-butoxide, present in slight molar excess to the sugar. At low temperature, 115°, a mixture of the N-alkoxycarbonyl compound (XXVI or XXX) and the N,O-di-alkoxycarbonyl compound (XXVII or XXXI) was formed. At high temperatures, 145°, the N-alkylated oxazolidone (XXIX or XXXII) was formed. These compounds were readily identifiable by IR-spectra because XXVI and XXX show the amide I and amide II bands; XXVII and XXXI show the ester, amide I and amide II bands; and XXIX and XXXII show only the characteristic oxazolidone band. The oxazolidone band is at the same frequency as the amide I band, but no amide II band appears.

The oxazolidone intermediate, XXVIII, was postulated due to the presence of the N-substituted product. Further evidence was found by substituting XXVIIIb (prepared by the method of Miyai and Gross[10]) for Ib and using the same high temperature reaction conditions. This reaction yielded

mostly the N-substituted oxazolidone, XXXIIb, with some XXXb and XXXIb. The equilibrium between XXXb, XXXIb, and XXVIIIb was more clearly established by substituting XXVIIIb for Ib using the same low temperature conditions, the product being a mixture of XXXb and XXXIb. No XXXIIb was found in this low temperature reaction, a fact which was further emphasized when XXXIIb was substituted for Ib under low temperature conditions and no reaction occured.

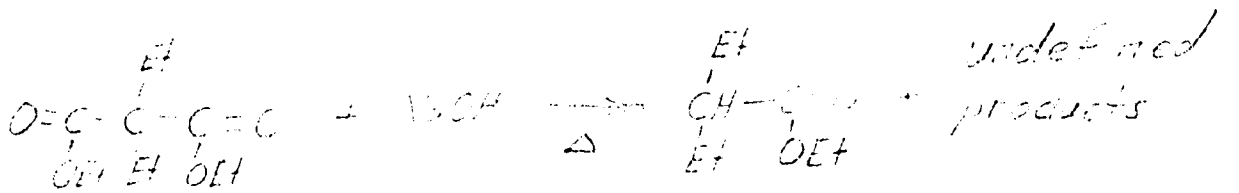
The above indicates that XXXb, XXXIb, and XXVIIIb exist at low temperature as an equilibrium mixture with the equilibrium shifted strongly toward XXXb and XXXIb. The N-substitution of the oxazolidone occurs only at high temperatures and is irreversible.

Benzyl 4,6-O-benzylidene-2-deoxy-2-(O-ethyl)malonamido-β-D-glucopyranoside (Vb) was then used in place of Ib. For both high temperature and low temperature reaction conditions the products yielded by Vb were the same as those yielded by Ib. These products can be explained by postulation that the oxazolidone XXVIIIb is formed by an internal hydroxyl attack on the amide carbonyl with subsequent loss of the remainder of the malonyl group. This leaves the oxazolidone intermediate which can immediately undergo the same reactions as when Ib was the starting material.



The above reaction is of interest in that it shows the preference of the hydroxyl group to attack the amide carbonyl (and form a five membered ring) rather than to attack the ester carbonyl, forming a seven membered ring. The apparent ease of reaction shows the stability of the five membered ring system, and suggests that any attempt to form a larger ring system using an amide under alkaline conditions will meet with failure. The reaction is unusual in that this is an example of an ester elimination which apparently has not been reported before. That such an elimination occurs so readily with these substances under mild conditions is readily explained by the favorable anchimeric assistance of the adjacent hydroxyl group.

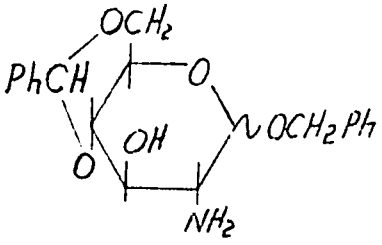
The conditions for the above reaction are in sharp contrast to the normal ester elimination. The ester elimination of malonic esters, and the relative ease of elimination of the dialkyl substituted esters, was first observed by Dieckmann[5] who correctly surmised the reaction to be:



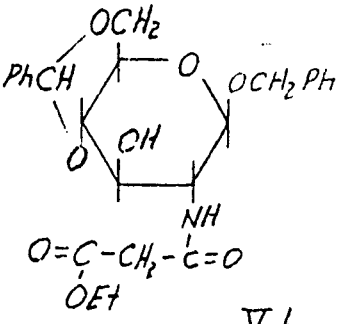
Quantitative studies by Cope and McElvain[4] showed that decarboxylation was easier as the number of C-alkyl substituents on the malonate increased. However, even the most easily decarboxylated malonate ester, the diethyl substituted, required thirty minutes with sodium ethoxide in ethanol at 250° and 1000 psi for 81% of the starting material to be decarboxylated.

The yields for the high temperature sugar reaction are quite high and could be used for a convenient single step procedure producing the N-substituted oxazolidones in much better yield then by preparation and subsequent alkylation of the unsubstituted oxazolidones reported by Miyai and Gross[10].

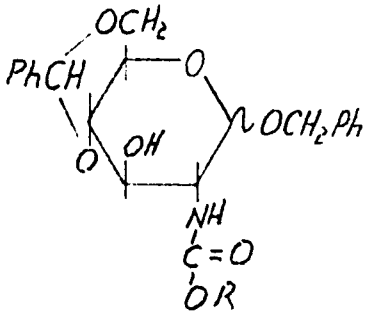
TABLE 5



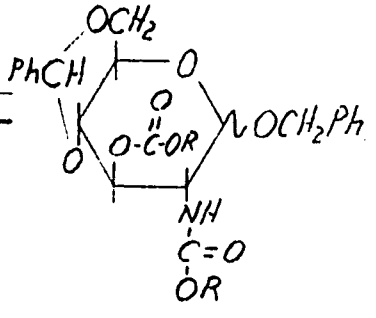
Ia
Ib



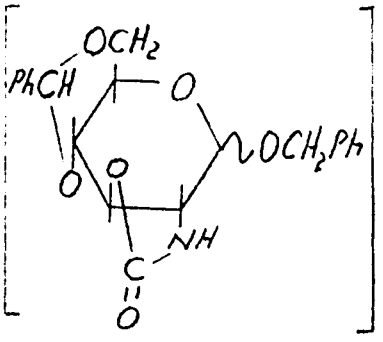
Vb



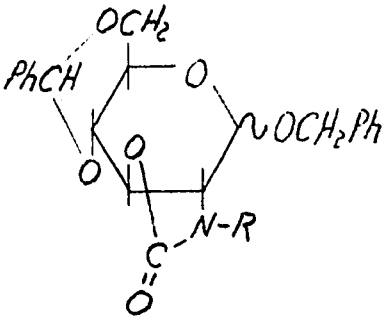
XXVIa
XXVIb } R=Me
XXXa
XXXb } R=Et



XXVIIa
XXVIIb } R=Me
XXXIa
XXXIb } R=Et



XXVIIIa
XXVIIIb



XXIXb ; R=Me
XXXIIa
XXXIIb } R=Et

CHAPTER V

DIFUNCTIONAL ADDITION OF DIFUNCTIONAL ESTERS

The possibility was considered of using a difunctional reagent, in a single reaction mixture, to react with both the alcohol and amine functional groups of compound I. This would give rise to a heterocyclic ring fused into the sugar ring. An attempt was made by reacting malonyl dichloride with I in a very dilute chloroform solution, with collidine to catalyze the reaction and neutralize the HCl formed. Both Ia and Ib yielded products (XXXIIIa and XXXIIIb) which showed no ester band in their IR-spectrum, but showed amide I and amide II bands. The presence of an amide II band was an indication that the amide group was not in a cyclic structure[1]. The IR-spectra also showed that the -OH band remained. The above data were in accord with dimerization having occured, the two sugars being linked by the malonyl attached at the 2-N position. The above IR-spectra provided strong evidence for dimerization, but no direct chemical operation on XXXIII to provide additional proof was evident and due to the compounds' relative insolubility, a Rast molecular weight determination could not be performed. Also, the IR evidence can not be considered as definitive, as larger rings do have an amide II band, and the possible heterocyclic structure would be a

seven membered ring with two carbonyl groups present. This could be a borderline case.

To assure that XXXIII was the dimer, the following procedure was used. Both XXXIIIa and XXXIIIb were synthesized by an independent method. An equimolar mixture of Ia and IVa were refluxed in xylene, yielding a single product identical to XXXIIIa, having $[\alpha]_D^{20}$ +109°. Similarly, Ib and IVb yielded a single product identical to XXXIIIb, having $[\alpha]_D^{20}$ -101°. While this provides considerable proof for the dimer structure, further confirmation can be obtained. If Ia and IVb are reacted together, they should yield a product identical to that obtained by reacting Ib and IVa together. This can be determined by drawing the structures of the two products and moving them through allowed operations on paper until they are identical. Furthermore, as the compound contains an α and a β sugar, and no new sites of asymmetry have been introduced, the specific rotation of this compound should lie half-way between the specific rotations of XXXIIIa and XXXIIIb. Both the above reactions were carried out yielding a single product, XXXIV, with $[\alpha]_D^{20}$ +3°. This is 1° from the average value of XXXIIIa and XXXIIIb.

The reactions between the acid dihalides and the glucosamine anomers were carried out under a range of temperatures from -15°C to 60°C, and in the solvents chloro-

form and tetrahydrafuran. The concentration of both reactants in the reaction mixture was kept to a minimum by the dropwise addition of solutions of both the acid dihalide and the sugar over a period of several hours. At all times the acid halide was in excess to the sugar. In none of these reactions was any product other than the dimer observed. In view of this, it may be said that the possibility is very low of forming any glucosamine protective heterocyclic group between positions 2 and 3 in a single reaction.

However, this does not mean that such heterocyclic groups can not be formed. A two step procedure is indicated in which a difunctional compound is first reacted selectively to the amine, the resulting compound is separated and purified, and finally the remaining functional group is reacted with the sugar's alcohol group. As in the final reaction there are no amine groups present, the competition is simply between an intra-alcohol attack (to form a heterocyclic) and an inter-alcohol attack (to form an oxygen-nitrogen linked dimer). In dilute solutions, the intramolecular attack should be favored, and the heterocyclic formed.

The necessary compounds for a two-step heterocyclic ring fusion to the sugar are available and have been discussed in Chapter 1. By refluxing in xylene, with a

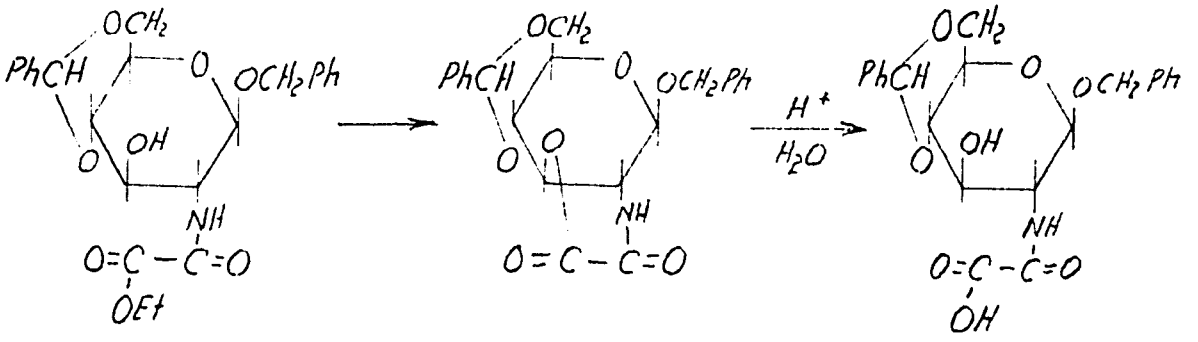
catalytic amount of base, it has been possible to convert IIIb into a six membered heterocyclic fused sugar, XXXV. However, this compound is quite sensitive and under slightly acidic conditions (such as being spotted on silica gel) degrades to give a compound which has an extremely low R_f value on silica gel. Due to this lack of TLC migration, the degradation product is interpreted as the oxalate half-acid, XXXVIb. That XXXVb has actually been formed can be demonstrated in two ways. The IR-spectra of XXXV shows strong, sharp ester and amide I bands, but no trace of an amide II band. On cellulose TLC, with pure chloroform as the solvent, XXXV has an R_f value of 0.7, much greater than IIIb, and indicating that no polar functional groups, such as an amine or alcohol, are present. The instability of the compound is attributed to ring strain plus the inductive effect of the adjacent consecutive carbonyl groups weakening the O-C bond in the ring. This morpholinedione ring is not new, having recently been reported by Drefahl, Hartmann and Skurk as fused into the cyclohexane ring[6]. This method of preparation is entirely analogous to their reported method. The cyclohexane fused heterocyclic compound is apparently more stable than XXXV.

A similar heterocyclic product could not be formed with IIIa. It is possible that the axial α glycosidic linkage forces this sugar ring further into a 1-C configuration, which precludes the formation of an already

sensitive heterocyclic ring system. Also, similar conditons with Va and Vb resulted in no reaction. A possible explanation for this is that the malonyl esters are much less reactive than the oxalyl esters.

TABLE 6

TABLE 6 (CONTINUED)



IIIb XXXVb XXXVIb

CHAPTER VI

SUMMARY AND CONCLUSIONS

A wide variety of benzyl 2-acylamido-2-deoxy-D-glucopyranosides has been synthesized by methods not previously used for sugars. Increasing difficulty in producing derivatives with bulky amide groups has been noted. The competition between ester elimination, to form amides, and amine attack of double bonds, to form secondary amines, has been studied. This latter reaction has resulted in new N-substituted glucosamines. A relationship between the IR-spectra amide I and amide II shifts and α-β isomerism has been discovered for the compounds studied. The relationship is that the amide bands of the α anomers of 3-position unsubstituted glucopyranosides are of lower wave number than the corresponding β anomers.

The stability of the formamide, oxamide, and malonamide groups with regard to acylations and debenzylidenations has been studied. The formamide and malonamide have been found to be quite stable, with the oxamide much less so. An exception with the formamides is mesylation, which gives rise to the dehydration of the formamide group to the isocyanide group. This is the first reported case of the introduction of an isocyanide group into a sugar, and the first reported case of using methanesulfonyl

chloride for the dehydrating agent to form an isocyanide. The sodium salt of the ethyl malonamide sugar has been formed. It has been found that the carbanion is formed, rather than saponification of the ester to form the sodium salt of the acid.

A series of N-substituted alkyl carbonates, N,O-di-substituted alkyl carbonates, oxazolidones, and N-substituted oxazolidone derivatives of glucosamine has been made and the equilibria (and irreversible reactions) between these species studied. This has resulted in an improved, and direct, route to the synthesis of N-substituted oxazolidones derived from D-glucosamine. In the course of these reactions a new type of ester elimination has been observed.

It has been found that on reacting with both functional groups of difunctional reagents glucosamines can follow two general paths. One possibility is for each mol of difunctional reagent to react with two mols of glucosamine to form a dimer. This has been shown to occur with malonyl dichloride and diethyl malonate to yield α-α, β-β, and α-β dimers. Dimers of this type have not been reported before. The second pathway is an intramolecular reaction with the difunctional reagent attacking the 2-amino group and the 3-hydroxyl group of a single glucosamine to form a heterocyclic ring fused into the sugar. This has been done with ethyl oxalate in a two step reaction to yield the

morpholinedione ring. This ring has been prepared before, but not fused into a sugar. This heterocyclic glucosamine derivative has not proven to be stable under mildly acidic conditons.

CHAPTER VII

EXPERIMENTAL PROCEDURE

The major analytical tools for monitoring the following reactions have been infrared spectra analysis and thin layer chromatography. The infrared spectra have been taken with a Perkin-Elmer 337 spectrophotometer using potassium bromide pellets. The TLC studies have been done with a mixture of two parts Merk Silica Gel G with one part Merk Silica Gel GF_{254}, the plates being activated by heating at 120^{o} for two hours. The plates were developed with chloroform, containing lesser amounts of either ethanol or petroleum ether. The compounds were visualized by extinction of the uv-fluoresence, and by spraying with a 20% sulfuric acid in methanol solution and heating for 10 minutes at 250^{o}. As absolute R_f values for TLC are difficult to determine, comparative studies have been made between various products and these reported separately. The preparative TLC separations were made on Merk precoated silica gel plates, 2 mm thick. The melting points are uncorrected and were taken on a Hoover-Thomas Uni-melt apparatus. The rotations were taken with a Rudolph polarimeter, model 956, in pyridine at c=1. The elemental analyses were determined by Alfred Bernhardt Mikroanalytisches Laboratorium, Engelskirchen, Germany. The commerical solvents and reagents were purified by fractional distillation.

The preparation of I can be found in references 1, 2 and 3. However, the modification of the final hydrolysis is reported here.

Benzyl 2-amino-4,6-O-benzylidene-2-deoxy-β-D-glucopyranoside (Ib):

To a refluxing solution of potassium hydroxide (105 g) in 95% ethanol (350 ml) was added benzyl 3-O-acetyl-4,6-O-benzylidene-2-benzyloxycarbonylamido-2-deoxy-β-D-glucopyranoside (27.5 g). The resulting solution was refluxed and stirred 6 hr, poured into 80°C water (2,800 ml) and filtered after 12 hr at 0°. The precipitate was dissolved in boiling methanol (400 ml), filtered hot and recrystallized. The resulting crystals were filtered out, air dried, and dissolved in boiling toluene (300 ml). Approximately 30 ml of toluene were distilled off. The toluene solution, after 12 hr at 0°, was filtered to yield Ib, 17.7 g (98%), physical constants identical to the compound reported by Gross and Jeanloz[3].

Identical conditions were used for the α-anomer, resulting in a similar yield.

Benzyl 4,6-O-benzylidene-2-deoxy-2-formamido-α-D-glucopyranoside (IIa):

A solution of Ia (5 g, 0.014 mol) and methyl formate (6 ml, 0.1 mol) in 0.1 N methanolic sodium methoxide (350 ml) was refluxed and stirred 5 hr, and the resulting solution kept 8 hr at 0°. The resulting crystals were filtered and recrystallized from dioxane/isopropanol to give 5.1 g (94%), m.p. 267-8°, $[\alpha]_D^{20}$ +99°. $\bar{\nu}_{max}(cm^{-1})$: 3390(m) → -OH; 3290(s) → -NH; 1650(s), 1530(s) → -NHCO-; 749(s), 697(s) → C_6H_5.

Analysis for $C_{21}H_{23}NO_6$ (385.40)

Calc.:	C	65.51	H	6.02	N 3.64
Found:	C	64.57	H	6.43	N 3.75

Benzyl 4,6-O-benzylidene-2-deoxy-2-formamido-β-D-glucopyranoside (IIb):

Compound Ib, by the same procedure as for IIa, gave 5.05 g (93%), m.p. 257-8°, $[\alpha]_D^{20}$ -70°. $\bar{\nu}_{max}(cm^{-1})$: 3390(m) → -OH; 3270(s) → -NH; 1670(s), 1550(s) → -NHCO-; 750(m), 697(m) → C_6H_5.

Analysis for $C_{21}H_{23}NO_6$ (385.40)

Calc.:	C	65.51	H	6.02	N 3.64
Found:	C	65.51	H	6.16	N 3.51

Benzyl 4,6-O-benzylidene-2-deoxy-2-(ethyl)oxamido-α-D-glucopyranoside (IIIa):

A solution of Ia (4 g, 0.011 mol) and diethyl oxalate (12 ml, 0.08 mol) in anhydrous ethanol (120 ml) was refluxed 12 hr, filtered hot, and kept 12 hr at -15°C. The resulting crystals were filtered and recrystallized from anhydrous ethanol to give 4.15 g (84%), m.p. 223-4°, $[\alpha]_D^{20}$ +88°.

$\bar{\nu}_{max}(cm^{-1})$: 3470(m) → -OH; 3300(s) → -NH; 1740(s) → -COOR; 1670(s), 1540(m) → -NHCO-; 745(m), 692(m) → C_6H_5.

Analysis for $C_{24}H_{27}NO_8$ (457.47)

Calc.:	C	63.07	H	5.96	N 3.07
Found:	C	63.65	H	5.94	N 2.92

Benzyl 4,6-O-benzylidene-2-deoxy-2-(ethyl)oxamido-β-D-glucopyranoside (IIIb):

Compound Ib, by the same procedure as described for IIIa, gave 3.8 g (76%), m.p. 214-5°, $[\alpha]_D^{20}$ -89°.

$\bar{\nu}_{max}(cm^{-1})$: 3530(m), 3495(m) → -OH; 3300(s) → -NH; 1730(s) → -COOR; 1690(s), 1550(w) → -NHCO-; 750(m), 692(m) → C_6H_5.

Analysis for $C_{24}H_{27}NO_8$ (457.47)

Calc.:	C	63.07	H	5.96	N 3.07
Found:	C	63.68	H	5.80	N 3.07

The below shows the general preparation of the benzyl 4,6-O-benzylidene-2-deoxy-2-(acyl)amino-D-glucopyranosides. Unless changes in the preparation or product are noted under the specific compounds, this procedure holds for all the following amide formation reactions.

The carboxylic ester and Ia (or csp. Ib) were stirred and heated for the time and temperature given below. The resulting hot solution was treated with petroleum ether/diethyl ether 1:1 (20 ml/gm of starting sugar) and kept 12 hr at -15°. The precipitate was filtered off and recrystallized from dioxane/isopropanol. The resulting yields and properties are summarized below. Only one ester group reacted to form the amide.

Benzyl 4,6-O-benzylidene-2-deoxy-2-(O-methyl) malonamido-α-D-glucopyranoside (IVa):

Dimethyl malonate (10 ml, 0.06 mol) and Ia (3 g, 0.009 mol) at 115° for 75 min yielded 3.47 g (93%), m.p. 224-5°, $[\alpha]_D^{20}$ +118°. $\bar{\nu}_{max}(cm^{-1})$: 3450(m) → -OH; 3280(s) → -NH; 1730(s) → -COOR; 1620(s), 1540(s) → -NHCO-; 750(m), 691(m) → C_6H_5.

Analysis for $C_{24}H_{27}NO_8$ (457.47)

Calc.:	C	63.00	H	5.95	N	3.07	O 27.98
Found:	C	62.68	H	6.07	N	3.10	O 28.10

Benzyl 4,6-O-benzylidene-2-deoxy-2-(O-methyl) malonamido-β-D-glucopyranoside (IVb):

Dimethyl malonate (5 ml, 0.03 mol) and Ib (1 g, 0.003 mol) at 115° for 85 min yielded 1.1 g (89%), m.p. 243-4°, $[\alpha]_D^{20}$ -82°. $\bar{\nu}_{max}(cm^{-1})$; 3480(m) → -OH; 3250(m) → -NH; 1740(s) → -COOR; 1650(s), 1540(m) → -NHCO-; 752(m), 691(m) → C_6H_5.

Analysis for $C_{24}H_{27}NO_8$ (457.47)

Calc.:	C	63.00	H	5.95	N	3.07	O 27.98
Found:	C	63.89	H	6.16	N	3.13	O 27.31

Benzyl 4,6-O-benzylidene-2-deoxy-2-(O-ethyl) malonamido- α-D-glucopyranoside (Va):

Diethyl malonate (45 ml, 0.3 mol) and Ia (7 g, 0.02 mol) at 110° for 3 hr yielded 7.24 g (80%), m.p. 188-9°, $[\alpha]_D^{20}$ +102°. $\bar{\nu}_{max}(cm^{-1})$: 3450(m) → -OH; 3280(s) → -NH; 1730(s) → -COOR; 1620(s), 1540(s) → -NHCO-; 740(m), 690(m) → C_6H_5.

Analysis for $C_{25}H_{29}NO_8$ (471.46)

Calc.:	C	63.86	H	6.20	N	2.79	O 27.15
Found:	C	61.63	H	6.25	N	3.03	O 29.44
Monohydrate:	C	61.34	H	6.38	N	2.86	O 29.42

Benzyl 4,6-O-benzylidene-2-deoxy-2-(O-ethyl) malonamido- β-D-glucopyranoside (Vb):

Diethyl malonate (8 ml, 0.048 mol) and Ib (8 g, 0.024 mol) at 115° for 3 hr yielded 8.46 g (82%), m.p. 181-2°, $[\alpha]_D^{20}$ -75°. $\bar{\nu}_{max}(cm^{-1})$: 3450(m) → -OH; 3270(m) → -NH; 1740(s) → -COOR; 1650(s), 1540(m) → -NHCO-; 750(m), 692(m) → C_6H_5.

Analysis for $C_{25}H_{29}NO_8$ (471.46)

Calc.:	C	63.86	H	6.20	N	2.79	O 27.15
Found:	C	63.69	H	6.19	N	2.81	O 27.10

Benzyl 4,6-O-benzylidene-2-deoxy-2-(O-methyl) succinamido- α-D-glucopyranoside (VIa):

Dimethyl succinate (3.0 ml, 0.017 mol) and Ia (1.0 g, 0.0027 mol) at 155° for 9 hr. Petroleum ether (20 ml) was added. After 3 hr at 20° (at lower temp. the dimethyl succinate crystallizes out) the mixture was filtered to yield 0.65 g precipate, containing approx 25% Ia, which was purified by preparative TLC. The major fraction was recrystallized from isopropanol to yield 0.40 g (30%), m.p. 201-2°, $[\alpha]_D^{20}$ +96°. $\bar{\nu}_{max}(cm^{-1})$: 3380(m) → -OH; 3290(s) → -NH; 1720(s) → -COOR; 1630(s), 1530(s) → -NHCO-; 691(s) → C_6H_5.

Analysis for $C_{25}H_{29}NO_8$ (471.49)

Calc.:	C	63.68	H	6.20	N	2.97	O	27.15
Found:	C	63.28	H	6.47	N	3.01	O	27.22

Benzyl 4,6-O-benzylidene-2-deoxy-2-(O-ethyl) fumaramido- α -D-glucopyranoside (VIIa):

Diethyl fumarate (3 ml, 0.02 mol) and Ia (0.60 g, 0.002 mol) at 155° for 4 hr gave 0.44 g, which when separated on preparative TLC gave a major component which recrystallized from dioxane/isopropanol yielded 0.27 g (34%) m.p. 206-7°, $[\alpha]_D^{20}$ +104°. $\bar{\nu}_{max}(cm^{-1})$: 3400(s) → -OH; 3270(s) → -NH; 1690(s) → -COOR; 1630(s), 1530(s) → -NHCO-; 745(m), 690(s) → C_6H_5.

Analysis for $C_{26}H_{29}NO_8$ (483.49)

Calc.:	C	64.59	H	6.04	N	2.90	O 26.47
Found:	C	65.40	H	5.66	N	3.00	O 25.93

Benzyl 4,6-O-benzylidene-2-deoxy-2-(O-ethyl) fumaramido- β -D-glucopyranoside (VIIb):

Diethyl fumarate (5 ml, 0.03 mol) and Ib (1 g, 0.003 mol) at 115° for 53 min yielded 0.64 g (48%), m.p. 235-6°, $[\alpha]_D^{20}$ -75°. $\bar{\nu}_{max}(cm^{-1})$: 3450(m) → -OH; 3280(m), 3240(m) → -NH; 1740(s) → -COOR; 1640(s), 1540(m) → -NHCO-; 751(m), 691(m) → C_6H_5.

Analysis for $C_{26}H_{29}NO_8$ (483.49)

Calc.:	C	64.59	H	6.04	N	2.90	O 26.47
Found:	C	65.64	H	5.66	N	3.00	O 25.93

The reaction between benzyl 2-amino-4,6-0-benzylidene-2-deoxy-β-D-glucopyranoside (Ib) and diethyl maleate.

Diethyl maleate (5 ml, 0.03 mol) and Ib (1.0 g, 0.003 mol) were stirred at 155° for 5 hr. The product was precipitated by first adding 15 ml diethyl ether and then adding 15 ml petroleum ether. After 6 hr at 0°, 0.45 g was filtered out and separated by preparative TLC to give two fractions.

Benzyl 4,6-0-benzylidene-2-deoxy-2-(0-ethyl) maleamido-β-D-glucopyranoside (VIIIb):

The slowest moving fraction, recrystallized from dioxane/isopropanol, yielded 0.17 g (13%), m.p. 203-5°, $\bar{\nu}_{max}(cm^{-1})$: 3420(s) → -OH; 3280(s) → -NH; 1710(s) -COOR; 1640(s), 1510(m) → -NHCO-; 743(s), 690(s) → C_6H_5.

Analysis for $C_{26}H_{29}NO_8$ (483.49)

Calc.:	C	64.59	H	6.04	N	2.90	O 26.47
Found:	C	64.95	H	6.40	N	3.54	O 24.66

Benzyl 4,6-0-benzylidene-2-deoxy-2-(1,2-diethoxy-carbonyl)ethylamino-β-D-glucopyranoside (IXb):

The fastest component, recrystallized from diisopropyl ether/petroleum ether, yielded 0.11 g (8%), m.p. 74-96°. Two slightly separated components on TLC due to the new asymmetric carbon at the amino group. $\bar{\nu}_{max}(cm^{-1})$:

3550(w) ⟶ -OH; 3210(w) ⟶ -NH; 1710(s), 1700(m) ⟶ -COOR; 750(m), 690(s) ⟶ C_6H_5.

Analysis for $C_{28}H_{35}NO_9$ (529.59)

Calc.:	C	63.51	H	6.66	N	2.64	O	27.19
Found:	C	63.30	H	6.59	N	2.96	O	27.22

Benzyl 4,6-O-benzylidene-2-deoxy-2-(2-ethoxycarbonyl) ethylamino-β-D-glucopyranoside (Xb):

Ethyl acrylate (6.0 ml, 0.06 mol) and Ib (0.80 g, 0.0022 mol) at 115° for 2.5 hr yielded 0.57 g. Purified by preparative TLC and recrystallized from isopropanol the major fraction yielded 0.42 g (41%), m.p. 114-5°, $[\alpha]_D^{20}$-68°.

$\bar{\nu}_{max}(cm^{-1})$: 3450(m) ⟶ -OH; 3300(w) ⟶ -NH; 1720(s) ⟶ -COOR; 761(m), 698(m) ⟶ C_6H_5.

Analysis for $C_{25}H_{30}NO_7$ (457.50)

Calc.:	C	65.63	H	6.83	N	3.06	O	24.48
Found:	C	65.27	H	6.60	N	3.42	O	24.78

Benzyl 3-O-acetyl-4,6-O-benzylidene-2-deoxy-2-formamido-α-D-glucopyranoside (XIa):

To a solution of IIa (1.5 g, 0.0039 mol) in dry pyridine (33 ml) was added acetic anhydride (1.8 ml, 0.017 mol). After 14 hr at 20°, ice and water (100 ml) was added to the reaction mixture. After 3 hr the precipitate was filtered off and recrystallized from dioxane/diisopropyl ether to give 1.37 g (77%), m.p. 194-5°, $[\alpha]_D^{20}$ +72°.

$\bar{\nu}_{max}(cm^{-1})$: 3270(s) → -NH; 1730(s) → -COOR; 1650(s), 1530(m) → -NHCO-; 751(m), 697(m) → C_6H_5.

Analysis for $C_{20}H_{25}NO_9$ (423.41)

Calc.:	C	64.69	H	5.90	N 3.28
Found:	C	64.41	H	6.02	N 3.12

Benzyl 3-O-acetyl-4,6-O-benzylidene-2-deoxy-2-formamido-β-D-glucopyranoside (XIb):

The above procedure was repeated with IIb (1.5 g) to give 1.32 g (74%), m.p. 287-8°, $[\alpha]_D^{20}$ -100°. $\bar{\nu}_{max}(cm^{-1})$: shows the same bands as given for XIa.

Analysis for $C_{20}H_{25}NO_9$ (423.41)

Calc.:	C	64.69	H	5.90	N 3.28
Found:	C	64.53	H	6.07	N 3.08

Benzyl 3-O-acetyl-2-deoxy-2-formamido-β-D-glucopyranoside (XIIb):

To a solution of XIb (1.06 g, 0.0022 mol) in acetic acid (20 ml) at 75° was added water (8 ml), dropwise over a 30 min interval. The solution was then evaporated *in vacuo* to dryness. To the residue was added water (two 10 ml portions), and then toluene (two 10 ml portions). After each solvent addition the solution was again evaporated to dryness *in vacuo*. The residue was then recrystallized from dioxane/diisopropyl ether to yield 0.62 g (77%), m.p. 192-3° $[\alpha]_D^{20}$ -66°. $\bar{\nu}_{max}(cm^{-1})$: 3420(s) → -OH; 3290(s) → -NH; 1700(s) → -COOR; 1660(s), 1530(m) → -NHCO-; 740(m), 693(m) → C_6H_5.

Benzyl 2-deoxy-2-formamido- α-D-glucopyranoside (XIVa):

To a mixture of IIa (0.92 g, 0.0024 mol) and acetic acid (35 ml) at 75° was added water (8 ml) dropwise over a 15 min interval. After the solution became clear it was evaporated *in vacuo* to dryness. To the residue was added water (two 10 ml portions) and then toluene (two 10 ml portions). After each solvent addition the solution was again evaporated *in vacuo* to dryness. The residue was recrystallized from dioxane/benzene to yield 0.51 g (72%), m.p. 148-9°, $[\alpha]_D^{20}$ +221°. $\bar{\nu}_{max}(cm^{-1})$: 3450(s), 3320(s) ⟶ -OH; 3200(s) ⟶ -NH; 1630(s), 1530(m) ⟶ -NHCO-; 750(s), 691(m) ⟶ C_6H_5.

Analysis for $C_{14}H_{19}NO_6$ (297.30)

Calc.:	C	56.61	H	6.45	N	4.72	O	32.32
Found:	C	56.60	H	6.51	N	4.78	O	32.47

Benzyl 2-deoxy-2-formamido- β-D-glucopyranoside (XIVb):

The above procedure was repeated with IIb (0.90 g) to yield 0.47 g (66%), m.p. 163-5°, $[\alpha]_D^{20}$ -56°. $\bar{\nu}_{max}(cm^{-1})$: 3450(s), 3340(s) ⟶ -OH; 3210(s) ⟶ -NH; 1650(s), 1540(s) ⟶ -NHCO-; 750(s), 695(s) ⟶ C_6H_5.

Benzyl 3,4,6-O-triacetyl-2-deoxy-2-formamido-α-D-glucopyranoside (XVa):

To a solution of XIVa (0.25 g, 0.00059 mol) in dry pyridine (2.0 ml) was added acetic anhydride (0.5 ml, 0.005 mol). After 12 hr at 25°, ice and water (20 ml) was added to the reaction mixture. After 4 hr the precipitate was filtered off and recrystallized from isopropanol to yield 0.33 g (92%), m.p. 113-4°, $[\alpha]_D^{20}$ +89°. $\bar{\nu}_{max}(cm^{-1})$: 3220(m) → -NH; 1730(s) → -COOR; 1660(s), 1530(m) → -NHCO-; 740(m), 696(w) → C_6H_5.

Analysis for $C_{20}H_{25}NO_9$ (423.41)

Calc.:	C	56.78	H	5.96	N 3.31
Found:	C	56.47	H	6.15	N 2.82

Benzyl 3,4,6-O-triacetyl-2-deoxy-2-formamido-β-D-glucopyranoside (XVb):

The above procedure was repeated with XIVb (0.25 g) to yield 0.31 g (87%), m.p. 170-1°, $[\alpha]_D^{20}$ -34°. $\bar{\nu}_{max}(cm^{-1})$ 3210(m) → -NH; 1730(s) → -COOR; 1660(s), 1510(m) → -NHCO-; 750(m), 698(m) → C_6H_5.

Analysis for $C_{20}H_{25}NO_9$ (423.41)

Calc.:	C	56.78	H	5.96	N 3.31
Found:	C	56.51	H	5.95	N 2.98

The reaction between benzyl 4,6-O-benzylidene-2-deoxy-2-formamido- α-D-glucopyranoside (IIa) and methane sulfonyl chloride.

To a mixture of IIa (1.5 g, 0.0039 mol) in dry pyridine (12 ml) at -10°, was added methane sulfonyl chloride (1.2 ml, 0.01 mol) dropwise over a 10 min interval. After 11 hr at 0° a clear solution with a deep red color resulted. Ice and water (40 ml) was added to the reaction mixture and a reddish precipitate resulted. After 4 hr at 5° the precipitate was filtered off, air dried, and recrystallized from dioxane/diisopropyl ether to yield 1.13 g. Analysis of this precipitate on TLC showed three major components, the red material which did not move from the origin plus two moving fractions. The mixture was then separated by preparative TLC using 2% ethanol in chloroform.

Benzyl 4,6-O-benzylidene-2-deoxy-2-isonitryl-3-mesyl-α-D-glucopyranoside (XVIa):

The fastest moving fraction, recrystallized from isopropanol/diisopropyl ether, yielded 0.21 g (12%), m.p. 176-7°, $[\alpha]_D^{20}$ +106°. $\bar{\nu}_{max}(cm^{-1})$: 2140(m) ⟶ -N≡C; 747(m), 696(m) ⟶ C_6H_5.

Analysis for $C_{22}H_{23}NO_7S$ (445.48)

Calc.:	C	59.31	H	5.20	N	3.15	O 25.14
Found:	C	60.10	H	5.30	N	3.02	O 25.49

Benzyl 4,6-O-benzylidene-2-deoxy-2-formamido-3-mesyl-α-D-glucopyranoside (XVIIa):

The slowest moving fraction to leave the origin, recrystallized from isopropanol, yielded 0.69 g (35%), m.p. 195-6°, $[\alpha]_D^{20}$ +67°. $\bar{\nu}_{max}(cm^{-1})$: 3270(s) ⟶ -NH; 1650(s), 1530(m) ⟶ -NHCO-; 741(s), 695(s) ⟶ C_6H_5.

Analysis for $C_{22}H_{25}NO_8S$ (463.49)

Calc.:	C	57.07	H	5.44	S 6.93
Found:	C	57.07	H	5.56	S 7.00

The reaction between benzyl 4,6-O-benzylidene-2-deoxy-2-formamido-β-D-glucopyranoside (IIb) and methane sulfonyl chloride.

The procedure was the same as for the above α anomer, however, using 7 hr reaction time instead of 11 hr. The reaction mixture also yielded a reddish precipitate (0.99 g) with two moving components on TLC.

Benzyl 4,6-O-benzylidene-2-deoxy-2-isonitryl-3-mesyl-β-D-glucopyranoside (XVIb):

The fastest moving fraction, recrystallized from isopropanol/diisopropyl ether, yielded 0.17 g (9%), m.p. 160-3°, $[\alpha]_D^{20}$ -46°. $\bar{\nu}_{max}(cm^{-1})$: 2140(m) ⟶ -N≡C; 741(m), 692(m) ⟶ C_6H_5. As both TLC and IR showed a trace of XVIIb, estimated at 5%, this compound has not been sent for analysis.

Benzyl 4,6-O-benzylidene-2-deoxy-2-formamido-3-mesyl-β-D-glucopyranoside (XVIIb):

The slowest moving fraction, recrystallized from isopropanol, yielded 0.72 g (37%), m.p. 180-1°, $[\alpha]_D^{20}$ -54°. $\bar{\nu}_{max}(cm^{-1})$: 3340(m) ⟶ -OH; 1660(s), 1520(s) ⟶ -NHCO-; 745(m), 698(m) ⟶ C_6H_5.

Analysis for $C_{22}H_{25}NO_8S$ (469.49)

Calc.:	C	57.07	H	5.44	N	3.03	S	6.93
Found:	C	57.48	H	5.62	N	2.83	S	6.51

Benzyl 3-O-acetyl-4,6-O-benzylidene-2-deoxy-2-(O-ethyl)malonamido- α-D-glucopyranoside (XVIIIa):

To a solution of Va (0.90 g, 0.0019 mol) in dry pyridine (8 ml) was added acetic anhydride (1.5 ml, 0.014 mol). After 10 hr at 25°, ice and water (40 ml) was added to the reaction mixture. After 6 hr the precipitate was filtered off, air dried, and recrystallized from isopropanol to yield 0.77 g (79%), m.p. 166-9°, $[\alpha]_D^{20}$ +210°. $\bar{\nu}_{max}(cm^{-1})$: 3280(s) ⟶ -NH; 1730(s) ⟶ -COOR; 1640(s), 1530(m) ⟶ -NHCO-; 751(m), 694(m) ⟶ C_6H_5.

Analysis for $C_{27}H_{31}NO_9$ (514.53)

Calc.:	C	62.97	H	6.07	N 2.72
Found:	C	63.13	H	5.90	N 2.91

Benzyl 3-O-acetyl-4,6-O-benzylidene-2-deoxy-2-(O-ethyl)malonamido- β-D-glucopyranoside (XVIIIa):

The above procedure was repeated with Vb (0.90 g) to yield 0.73 g (74%), m.p. 188-9°, $[\alpha]_D^{20}$ -93°. $\bar{\nu}_{max}(cm^{-1})$: 3280(s) ⟶ -NH; 1730(s) ⟶ -COOR; 1640(s), 1530(m) ⟶ -NHCO-; 751(m), 694(m) ⟶ C_6H_5.

Analysis for $C_{27}H_{31}NO_9$ (514.53)

Calc.:	C	62.97	H	6.07	N 2.72
Found:	C	62.66	H	6.52	N 2.38

Benzyl 2-deoxy-2-(O-ethyl)malonamido-α-D-glucopyranoside (XXa):

To a solution of Va (0.81 g, 0.0017 mol) and acetic acid (25 ml) at 75° was added water (12 ml, 0.7 mol) dropwise over a 45 min interval. The solution was then evaporated *in vacuo* to dryness. To the residue was added water (two 10 ml portions) and then toluene (two 10 ml portions). After each solvent addition the solution was again evaporated *in vacuo* to dryness. The residue was then recrystallized from dioxane/benzene to yield 0.39 g (59%), m.p. 147-8°, $[\alpha]_D^{20}$ +157°. $\bar{\nu}_{max}(cm^{-1})$: 3530(m), 3380(s) ⟶ -OH; 3280(s) ⟶ -NH; 1730(s) ⟶ -COOR; 1630(s), 1530(s) ⟶ -NHCO-; 740(m), 692(m) ⟶ C_6H_5.

Analysis for $C_{18}H_{25}NO_8$ (383.39)

Calc.:	C	56.44	H	6.58	N	3.66	O 33.42
Found:	C	56.26	H	6.73	N	2.64	

Benzyl 2-deoxy-2-(O-ethyl)malonamido-β-D-glucopyranoside (XXb):

The above procedure was repeated with Vb (0.80 g) to gield 0.56 g (85%), m.p. 177-8°, $[\alpha]_D^{20}$ -27°. $\bar{\nu}_{max}(cm^{-1})$: 3360(s) ⟶ -OH; 3270(s) ⟶ -NH; 1730(s) ⟶ -COOR; 1660(s), 1540(s) ⟶ -NHCO-; 742(m), 693(m) ⟶ C_6H_5.

Analysis for $C_{18}H_{25}NO_8 \cdot H_2O$ (401.39)

Calc.:	C	53.85	H	6.78	N	3.49
Found:	C	54.26	H	6.73	N	3.58

Benzyl 3,4,6-O-triacetyl-2-deoxy-2-(O-ethyl) malonamido-α-D-glucopyranoside (XXIa):

To a solution of XXa (0.25 g, 0.0016 mol) and dry pyridine (2 ml) was added acetic anhydride (0.5 ml, 0.005 mol). After 10 hr at 25°, ice and water (20 ml) was added to the reaction mixture. First crystals developed, then oil. A system could not be found to crystallize the oil, 0.27 g (81%), uniform on TLC. $\bar{\nu}_{max}$(cm^{-1}): 3340(m) ⟶ -NH; 1740(s) ⟶ -COOR; 1670(m), 1530(m) ⟶ -NHCO-; 750(m), 695(m) ⟶ C_6H_5.

Benzyl 3,4,6-O-triacetyl-2-deoxy-2-(O-ethyl) malonamido-β-D-glucopyranoside (XXIb):

The above procedure was repeated with XXb (0.25 g) to give a precipitate, which recrystallized from isopropanol/diisopropyl ether yielded 0.22 g (67%), m.p. 159-60°, $[\alpha]_D^{20}$ -22°. $\bar{\nu}_{max}$(cm^{-1}): 3310(m) ⟶ -NH; 1730(s) ⟶ -COOR; 1660(s), 1520(m) ⟶ -NHCO-; 752(m), 692(m) ⟶ C_6H_5.

Analysis for $C_{24}H_{31}NO_{11}$ (509.50)

Calc.:	C	56.52	H	6.13	N 2.75
Found:	C	56.53	H	6.23	N 2.66

Benzyl 4,6-O-benzylidene-2-deoxy-2-(O-ethyl) malonamido-3-mesyl- α-D-glucopyranoside (XXIIa):

To a solution of Va (1.5 g, 0.0032 mol) in dry pyridine (12 ml) at -10°, was added methane sulfonyl chloride (1.2 ml, 0.01 mol) dropwise over a 15 min interval. After 14 hr at 0°, ice and water (80 ml) was added to the reaction mixture. After 4 hr at 5° the precipitate was filtered off, air dried, and recrystallized from dioxane/ diisopropyl ether to yield 1.51 g (86%), m.p. 190-1°, $[\alpha]_D^{20}$ +198°. $\bar{\nu}_{max}(cm^{-1})$: 3290(s) → -NH; 1730(s) → -COOR; 1650(s), 1540(s) → -NHCO-; 747(m), 691(m) → C_6H_5.

Analysis for $C_{26}H_{31}NO_{10}S$ (549.58)

Calc.:	C	56.77	H	5.68	N	2.55	S	5.83
Found:	C	56.74	H	5.61	N	2.50	S	6.02

Benzyl 4,6-O-benzylidene-2-deoxy-2-(O-ethyl) malonamido-3-mesyl- β-D-glucopyranoside (XXIIb):

The above procedure was repeated with Vb (1.5 g). Recrystallization from ethanol yielded 1.00 g (57%), m.p. 168-9°, $[\alpha]_D^{20}$ -48°. $\bar{\nu}_{max}(cm^{-1})$: 3260(s) → -NH; 1730(s) → -COOR; 1650(s), 1530(s) → -NHCO-; 749(m), 690(m) → C_6H_5.

Analysis for $C_{26}H_{31}NO_{10}S$ (549.58)

Calc.:	C	56.77	H	5.68	N	2.55	S	5.83
Found:	C	56.93	H	5.61	N	2.42	S	6.01

Benzyl 4,6-O-benzylidene-2-deoxy-2-(O-ethyl-C-sodium) malonamido-β-D-glucopyranoside (XXIIIb):

A solution of Vb (2.35 g, 0.005 mol), water (20 ml), methanol (20 ml) and dioxane (100 ml) was treated with a solution of sodium metal (0.127 g, 0.0055 mol) in methanol (11 ml) at 25°. The resulting solution was evaporated in vacuo. Dioxane and toluene were added to the residue and reevaporated in vacuo. The residue was dried for 1 hr at 80°, washed with chloroform/ether, and dried for 12 hr at 50°, yielding 2.31 g (98%), m.p. 264-5°. $\bar{\nu}_{max}(cm^{-1})$: 3410(m) → -OH; 3280(s) → -NH; 1710(s) → -COOR; 1640(s), 1530(s) → -NHCO-; 742(s), 691(s) → C_6H_5. Very slow migration on TLC compared to Vb when using chloroform/ethanol solution.

The starting material, Vb, used in the above reaction was regenerated in the following manner. To a mixture of XXIIIb (0.94 g, 0.002 mol) in methanol (100 ml) was added 0.23 N HCl (8 ml, 0.002 mol) and glacial acetic acid (2 drops). The solution was stirred rapidly for 5 hr, the precipitate dried azetropically with ethanol/toluene, and recrystallized from dioxane/isopropanol to yield 0.80 g (84%). Physical constants are identical to Vb (rotation, R_f value, IR-spectrum) with the exception that this product melts at 231-2°. A mixed melting point is half way between the new and old melting points. This is interpreted as being a new crystal form.

The reaction between benzyl 2-amino-4,6-O-benzylidene-2-deoxy- α-D-glucopyranoside (Ia) and dimethyl carbonate.

A solution of Ia (1.00 g, 0.0028 mol) in warm dimethyl carbonate (25 ml) was treated with potassium tert-butoxide (0.40 g, 0.0036 mol), stirred and refluxed for 12 hr, then filtered hot leaving a white residue (ppt. 1, 0.47 g). Petroleum ether (200 ml) was added to the filtrate, which was again filtered after 1.5 hr at 0° (ppt. 2, 0.69 g). this filtrate was evaporated in vacuo to dryness (ppt. 3, 0.23 g). Ppt. 2 and ppt. 3 were separated on preparative TLC; ppt. 2 yielded 0.23 g fast fraction and 0.27 g slow fraction, ppt. 3 yielded 0.15 g fast fraction and 0.03 g slow fraction.

Benzyl 4,6-O-benzylidene-2-deoxy-2-(methoxycarbonyl) amino- α-D-glucopyranoside (XXVIa):

The slowest moving fractions were combined and recrystallized from isopropanol to give 0.31 g (27%), m.p. 195-6°, $[\alpha]_D^{20}$ +114°. $\bar{\nu}_{max}$(cm^{-1}): 3380(m) ⟶ -OH; 3310(s) ⟶ -NH; 1670(s), 1530(s) ⟶ -NHCO-; 740(m), 691(m) ⟶ C_6H_5.

Analysis for $C_{22}H_{27}NO_7$ (415.41)

Calc.:	C	63.59	H	6.07	N	3.37	O	26.96
Found:	C	63.30	H	6.16	N	3.35	O	26.79

Benzyl 4,6-O-benzylidene-2-deoxy-3-O-methoxycarbonyl-2-(methoxycarbonyl)amino-α-D-glucopyranoside (XXVIIa):

The fastest moving fractions were combined and recrystallized from isoporpanol/diisopropyl ether to give 0.25 g (19%), m.p. 169-70°, $[\alpha]_D^{20}$ +71°. $\bar{\nu}_{max}(cm^{-1})$: 3300(s) → -NH; 1790(s) → -NHCO-; 1680(s), 1520(s) → -NHCO-; 732(s), 695(s) → C_6H_5.

Analysis for $C_{24}H_{27}NO_9$ (473.52)

Calc.:	C	60.88	H	5.75	N	2.96	O 30.41
Found:	C	60.80	H	5.58	N	2.87	O 30.65

The reaction between benzyl 2-amino-4,6-O-benzylidene-2-deoxy-β-D-glucopyranoside (Ib) and dimethyl carbonate.

A solution of Ib (1.00 g, 0.0028 mol) in warm dimethyl carbonate (25 ml) was treated with potassium tert-butoxide (0.40 g, 0.0036 mol), stirred and refluxed 7 hr, and filtered hot leaving a white basic residue (ppt. 1, 0.37 g). Petroleum ether (200 ml) was added to the filtrate. After 45 min at 0° ppt. 2 (0.96 g) was filtered out. The resulting filtrate was evaporated in vacuo to dryness (ppt. 3, 0.13 g).

Analytical TLC showed that ppt. 2 contained only two components and that ppt. 3 was a mixture of these same two components and two minor components with R_f values identical to XXVIIIb and XXIXb. Only ppt. 2 was separated by preparative TLC, giving two fractions.

Benzyl 4,6-O-benzylidene-2-deoxy-2-(methoxycarbonyl) amino-β-D-glucopyranoside (XXVIb):

The slowest moving fraction from the above separation was recrystallized from isopropanol to give 0.36 g (31%), m.p. 206-7°, $[\alpha]_D^{20}$ -89°. $\bar{\nu}_{max}(cm^{-1})$: 3400(m) → -OH; 3320(s) → -NH; 1680(s), 1530(s) → -NHCO-; 745(m), 692(m) → C_6H_5.

Analysis for $C_{22}H_{27}NO_7$ (415.41)

Calc.:	C	63.59	H	6.07	N	3.37	O 26.96
Found:	C	63.49	H	6.25	N	3.23	O 27.05

Benzyl 4,6-O-benzylidene-2-deoxy-3-O-methoxycarbonyl-2-(methoxycarbonyl)amino-β-D-glucopyranoside (XXVIIb):

From the above TLC separation of ppt. 2 the fastest moving component was recrystallized from isopropanol/diisopropyl ether to give 0.31 g (24%), m.p. 204-5°, $[\alpha]_D^{20}$ -101°. $\bar{\nu}_{max}$(cm^{-1}): 3320(s) → -NH; 1750(s) → -COOR; 1690(s), 1530(s) → -NHCO-; 749(s), 692(s) → C_6H_5.

Analysis for $C_{24}H_{27}NO_9$ (473.52)

Calc.:	C	60.88	H	5.75	N	2.96	O 30.41
Found:	C	60.79	H	5.67	N	3.02	O 30.44

Benzyl 4,6-O-benzylidene-2-deoxy-N-methyl-β-D-glucopyranosido-[2.3:4'.5'.]-2'-oxazolidone (XXIXb):

A solution of Ib (0.50 g, 0.0014 mol) in warm dimethyl carbonate (12 ml) was treated with potassium t-butoxide (0.20 g, 0.0018 mol), stirred in an autoclave 15 hr at 130°, and filtered hot leaving a white crystalline precipate (ppt. 1, 0.42 g). Petroleum ether (100 ml) was added to the filtrate which after 1 hr at 0° was again filtered (ppt. 2, 0.16 g). This filtrate was evaporated in vacuo to dryness and on TLC showed approximately equal portions of XXVIb, XXVIIb, and XXVIIIb (total wt. 0.20 g).

The solution of ppt. 1 and ppt. 2 in chloroform was extracted twice with ice cold 0.5 M HCl and once with 5% sodium bicarbonate, dried for 1 hr over anhydrous sodium carbonate and evaporated in vacuo to dryness. The solid residue (0.32 g) was recrystallized from ethanol to give 0.30 g (54%), $[\alpha]_D^{20}$ -101°, m.p. 258-9°. Mixed m.p. and IR spectra confirmed the identity with authentic XXIXb .

The reaction between benzyl 2-amino-4,6-O-benzylidene-2-deoxy- α-D-glucopyranoside (Ia) and diethyl carbonate.

A solution of Ia (1.00 g, 0.0028 mol) in warm diethyl carbonate (25 ml) was treated with t-butoxide (0.40 g, 0,0036 mol), stirred and heated 9 hr at 115°, then filtered hot leaving a white basic residue (ppt. 1, 0.47 g). Petroleum ether (200 ml) was added to the filtrate which was again filtered after 45 min at 0° (ppt. 2, 0.52 g). This filtrate was evaporated to dryness (ppt. 3, 0.23 g).

Analytical TLC showed that both ppt. 2 and ppt. 3 were mixtures of the same two components. However, in ppt. 2 the major component was slow moving, in ppt. 3 the major was fast moving. Ppt. 2 and ppt. 3 were separated by preparative TLC; ppt. 2 yielded 0.12 g fast fraction and 0.32 g slow fraction, ppt. 3 yielded 0.22 g fast fraction and 0.13 g slow fraction.

Benzyl 4,6-O-benzylidene-2-deoxy-2-(ethoxycarbonyl) amino- α-D-glucopyranoside (XXXa):

The slowest moving fractions were combined and recrystallized from isopropanol to give 0.40 g (35%), m.p. 197-8°, $[\alpha]_D^{20}$ +89°. $\bar{\nu}_{max}(cm^{-1})$: 3390(m) → -OH; 3300(s) → -NH; 1670(s), 1530(s) → -NHCO-; 745(m), 691(m) → C_6H_5.

Analysis for $C_{23}H_{27}NO_7$ (429.46)

Calc.:	C	64.31	H	6.33	N	3.27	O	26.08
Found:	C	63.60	H	6.36	N	3.24	O	26.74

Benzyl 4,6-O-benzylidene-2-deoxy-3-O-ethoxycarbonyl-2-(ethoxycarbonyl)amino-α-D-glucopyranoside (XXXIa):

The fastest moving fractions were combined and recrystallized from isopropanol/diisopropyl ether to give 0.29 g (22%), m.p. 138-9°, $[\alpha]_D^{20}$ +59°. $\bar{\nu}_{max}(cm^{-1})$: 3290(s) → -NH; 1730(s) → -COOR; 1670(s), 1520(s) → -NHCO-; 746(m), 690(m) → C_6H_5.

Analysis for $C_{26}H_{31}NO_9$ (501.52)

Calc.:	C	62.26	H	6.23	N	2.80	O	28.71
Found:	C	59.94	H	6.14	N	2.93	O	27.72

Benzyl 4,6-O-benzylidene-2-deoxy-N-ethyl-α-D-glucopyranosido-[2.3:4'.5'.]-2'-oxazolidone (XXXIIa):

A solution of Ia (1.00 g, 0.0028 mol) in warm diethyl carbonate (25 ml) was treated with potassium t-butoxide (0.40 g, 0.0036 mol), refluxed with stirring for 48 hr, and filtered hot leaving a basic precipitate (ppt. 1, 0.32 g). Petroleum ether (200 ml) was added to the filtrate, which was filtered again after 2 hr at 0° (ppt. 2, 0.30 g). Immediately after filtering white cyrstalline material came out of solution which after 1 hr at 0° yielded precipitate 3 (0.53 g). The solution was then evaporated to dryness in vacuo (ppt. 4, 0.31 g) which proved to be a mixture of XXXa, XXXIa, and XXXIIa. Ppt. 1 and ppt. 2 proved to be strongly basic. Ppt. 3 was found to be pure XXXIIa which when recrystallized from isopropanol/diisopropyl ether yielded 0.49 g (45%), m.p. 181-2°, $[\alpha]_D^{20}$ +46°. $\bar{\nu}_{max}(cm^{-1})$: 1740(s) ⟶ oxazolidone; 750(m), 696(m) ⟶ C_6H_5.

Analysis for $C_{23}H_{25}NO_6$ (411.44)

Calc.:	C	67.13	H	6.12	N	3.41	O	23.33
Found:	C	67.35	H	6.17	N	3.15	O	23.52

The reaction between benzyl 2-amino-4,6-O-benzylidene-2-deoxy-β-D-glucopyranoside (Ib) and diethyl carbonate.

A solution of Ib (1.00 g, 0.0028 mol) in warm diethyl carbonate (25 ml) was treated with potassium tert-butoxide (0.40 g, 0.0036 mol), stirred and heated 24 hr at 115°. then filtered hot leaving a basic residue (ppt. 1, 0.44 g). Petroleum ether (200 ml) was added to the filtrate, which was again filtered after 1 hr at 0° (ppt. 2, 0.55 g). The filtrate was evaporated in vacuo to dryness (ppt. 3, 0.53 g).

Benzyl 4,6-O-benzylidene-2-deoxy-2-(ethoxycarbonyl) amino-β-D-glucopyranoside (XXXb):

Precipitate 2, on recrystallization from dioxane/isopropanol, yielded 0.50 g (43%), m.p. 220-2°, $[\alpha]_D^{20}$ -87°. $\bar{\nu}_{max}(cm^{-1})$: 3430(m) ⟶ -OH; 3300(s) ⟶ -NH; 1680(s), 1530(s) ⟶ -NHCO-; 749(m), 692(m) ⟶ C_6H_5.

The above was identical to an authentic sample .

Benzyl 4,6-O-benzylidene-2-deoxy-3-O-ethoxycarbonyl-2-(ethoxycarbonyl) amino-β-D-glucopyranoside (XXXIb):

Precipitate 3, on recrystallization from ethanol, yielded 0.43 g (32%), m.p. 164-5°, $[\alpha]_D^{20}$ -85°. $\bar{\nu}_{max}(cm^{-1})$: 3320(s) ⟶ -NH; 1730(s) ⟶ -COOR; 1690(s), 1520(s) ⟶

-NHCO-; 750(s), 690(s) $\longrightarrow$ C_6H_5.

Analysis for $C_{26}H_{31}NO_9$ (501.52)

Calc.:	C	62.26	H	6.23	N	2.80	O	28.71
Found:	C	61.81	H	6.41	N	3.08	O	28.49

Benzyl 4,6-O-benzylidene-2-deoxy-N-ethyl-β-D-glucopyranosido-[2.3:4'.5'.]-2'-oxazolidone (XXXIIb):

A solution of Ib (0.50 g, 0.0014 mol) in warm diethyl carbonate (12 ml) was treated with potassium tert-butoxide (0.20 g, 0.0018 mol), was refluxed with stirring for 62 hr, and filtered hot leaving a precipitate (ppt. 1, 0.05 g). Petroleum ether (200 ml) was added to the filtrate, which was filtered again after 1 hr at 0° (ppt. 2, 0.15 g). The solution was then evaporated in vacuo to dryness (ppt. 3, 0.49 g).

Precipitate 3, shown by TLC to be XXXIIb with some XXXIb, was recrystallized from methanol (0° for 16 hr) to yield 0.41 g (75%), m.p. 200-1°, $[\alpha]_D^{20}$ -105°. $\bar{\nu}_{max}(cm^{-1})$: 1750(s) ⟶ oxazolidone; 760(m), 646(m) ⟶ C_6H_5.

Analysis for $C_{23}H_{25}NO_6$ (411.44)

Calc.:	C	67.13	H	6.12	N	3.41	O	23.33
Found:	C	67.24	H	6.15	N	3.45	O	23.30

Benzyl 4,6-O-benzylidene-2-deoxy-2-(2-amido benzyl 4,6-O-benzylidene-2-deoxy-α-D-glucopyranosido) malonamido-α-D-glucopyranoside (XXXIIIa):

Procedure 1

To a solution of dry, alcohol free chloroform (100 ml) and collidine (1.17 g, 0.007 mol) at -10° were added dropwise two separate solutions: Ia (0.98 g, 0.0027 mol) in chloroform (50 ml), and malonyl dichloride (0.46 g, 0.0033 mol) in chloroform (50 ml). At the start, 5 ml of the malonyl dichloride solution was added and the two solutions were then added at an equal rate over a 2 hr period. The reaction mixture was stirred for 4 hr (the temperature slowly rising to 20°), extracted successively with 5% aqueous $KHCO_3$, 5% citric acid, and distilled water. The chloroform phase was then dried over K_2CO_3 and evaporated *in vacuo*. The solid residue was recrystallized from dioxane/diisopropyl ether to yield 0.92 g (90%), m.p. 306-7° d, $[\alpha]_D^{20}$ +109°. $\bar{\nu}_{max}(cm^{-1})$: 3580(m) → -OH; 3280(s) → -NH; 1650(s), 1520(m) → -NHCO-; 734(s), 691(s) → C_6H_5.

Procedure 2

A solution of Ia (0.20 g, 0.00056 mol) and IVa (0.25 g, 0.00056 mol) in xylene (30 ml) was refluxed with stirring

for 14 hr. The precipitate formed was filtered hot from the solution, air dried, and recrystallized from dioxane/diisopropanol to yield 0.36 g (79%), physical constants identical to the product from procedure 1.

Benzyl 4,6-O-benzylidene-2-deoxy-2-(2-amido benzyl 4,6-O-benzylidene-2-deoxy-β-D-glucopyranosido) malonamido-β-D-glucopyranoside (XXXIIIb):

Procedure 1

Identical to procedure 1 of XXXIIIa except that Ib was used in place of Ia to yield 0.87 g (85%), m.p. 280-1° d, $[\alpha]_D^{20}$ -101°. $\bar{\nu}_{max}(cm^{-1})$: 3480(m) → -OH; 3270(s) → -NH; 1640(s), 1520(s) → -NHCO-; 745(s), 692(s) → C_6H_5.

Procedure 2

Identical to procedure 2 of XXXIIIa using the β anomers rather than the α anomers to yield 0.32 g (72%). The physical constants are identical to the product XXXIIIb of procedure 1.

Benzyl 4,6-O-benzylidene-2-deoxy-2-(2-amido benzyl 4,6-O-benzylidene-2-deoxy-α-D-glucopyranosido) malonamido-β-D-glucopyranoside (XXXIV):

Procedure 1

Identical to procedure 2 of XXXIIIa using Ib and IVa to yield 0.36 g (79%), m.p. 292-3° d, $[\alpha]_D^{20}$ +3°.

$\bar{\nu}_{max}$(cm^{-1}): 3380(m) ⟶ -OH; 3270(s) ⟶ -NH; 1640(s), 1540(m) ⟶ -NHCO-; 748(m), 692(m) ⟶ C_6H_5.

Procedure 2

Identical to procedure 2 of XXXIIIa using Ia and IVb to yield 0.28 g (62%). The physical constants are identical to the product from procedure 1.

Benzyl 4,6-O-benzylidene-2-deoxy-2,3-morpholinedione-β-D-glucopyranoside (XXXVb):

A solution of potassium t-butoxide (0.02 g, 0.0002 mol) and IIIb (0.51 g, 0.0012 mol) in xylene (20 ml) was refluxed for 6 hr. After 24 hr at 20°, dry ice was added. The reaction mixture was filtered through a short cellulose column, evaporated to dryness in vacuo, and recrystallized from chloroform/diisopropyl ether to yield 0.15 g (32%), m.p. 127-8°, $[\alpha]_D^{20}$ -79°. $\bar{\nu}_{max}(cm^{-1})$: 3480(m) → -NH; 1770(s) → -COOR; 1720(s) → -NHCO-; 755(m), 700(m) → C_6H_5.

Analysis for $C_{22}H_{21}NO_7$ (411.39)

Calc.:	C	64.21	H	5.15	N	3.41	O 27.22
Found:	C	64.18	H	5.40	N	3.30	O 27.31

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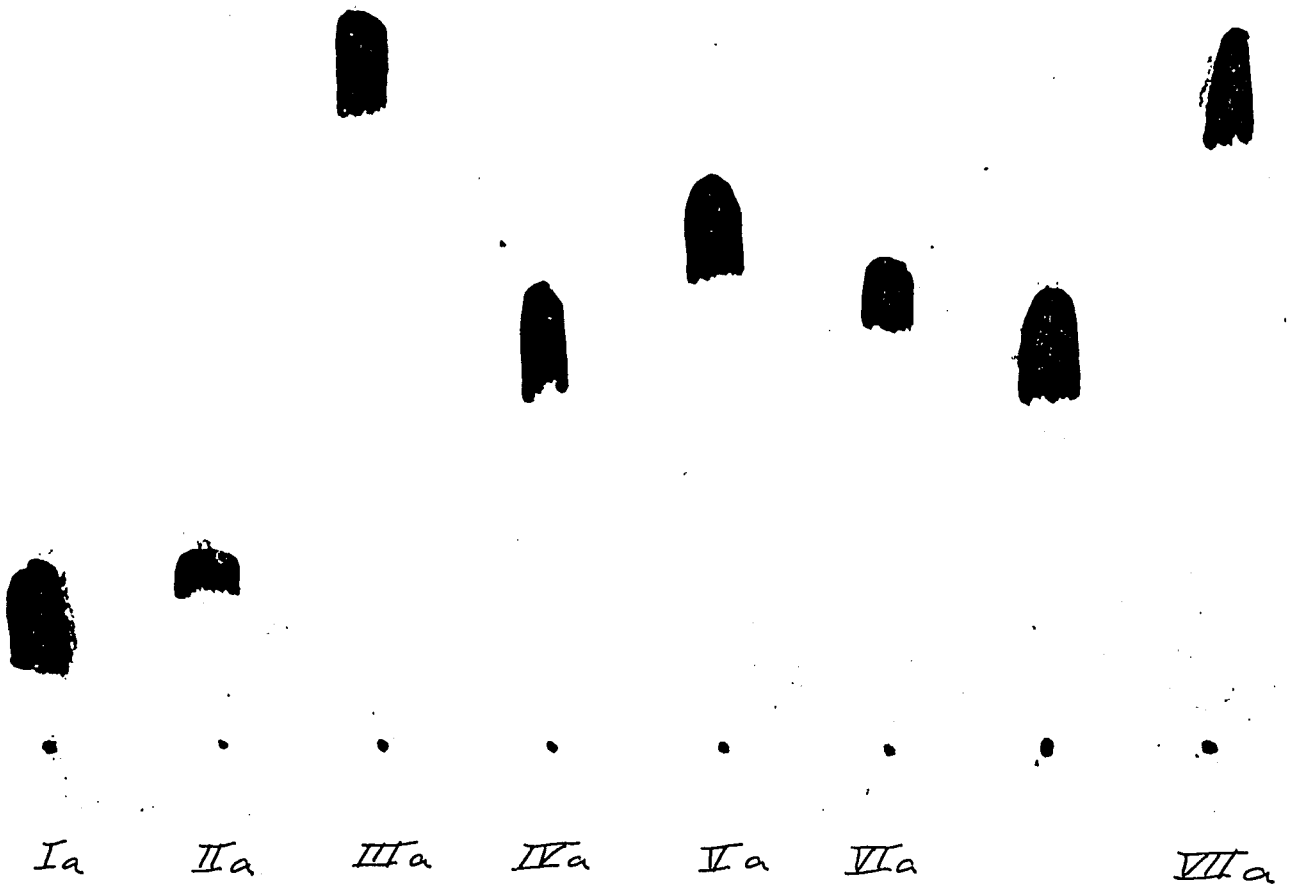
APPENDIX

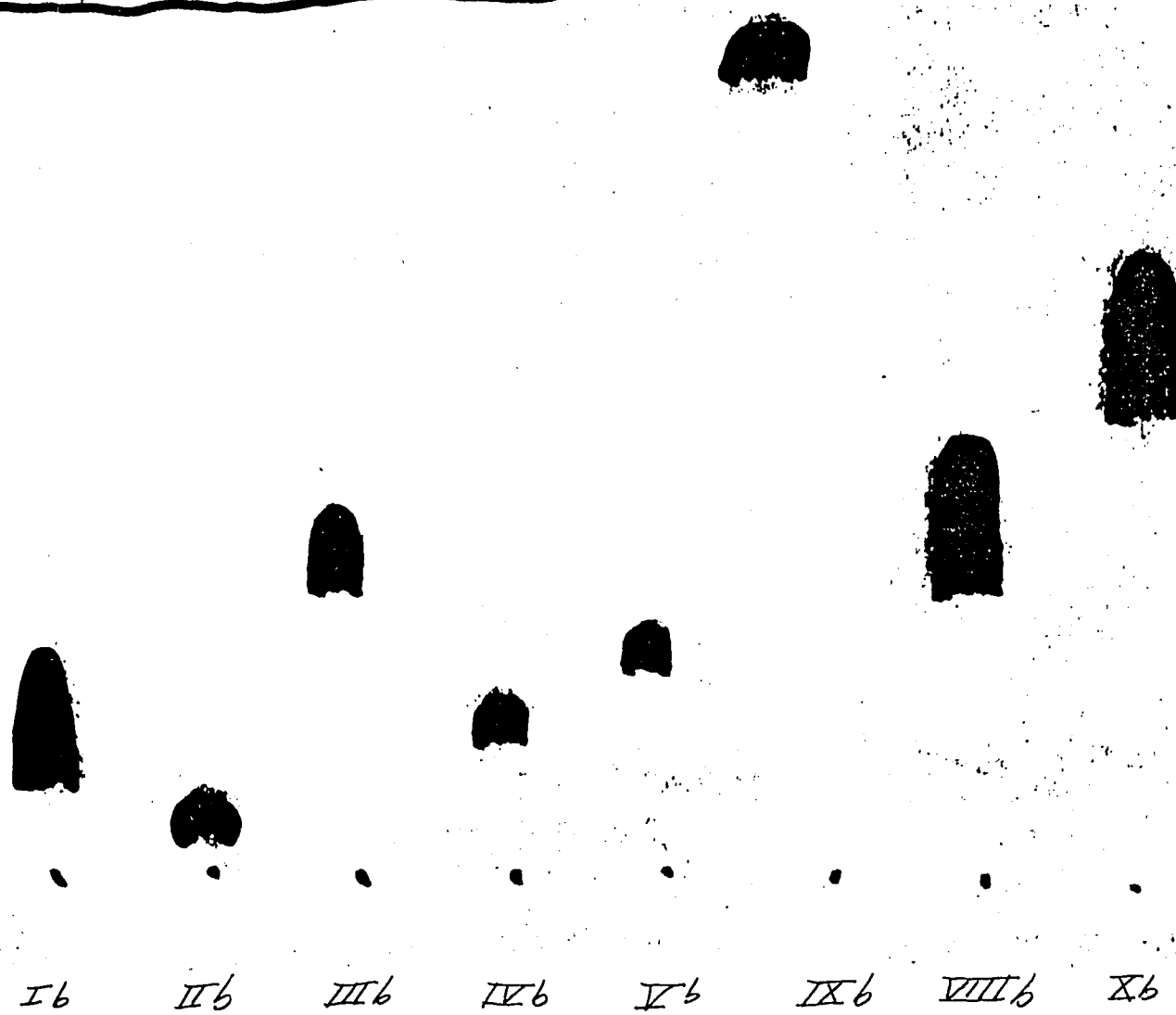


Ia: Benzyl 2-amino-4,6-0-benzylidene-2-deoxy- α-D-glucopyranoside

The remainder are derivatives of the above differing only at the 2 position.

IIa: 2-formamido
IIIa: 2-(0-ethyl)oxamido
IVa: 2-(0-methyl)malonamido
Va: 2-(0-ethyl)malonamido
VIa: 2-(0-methyl)succinamido
VIIb: 2-(0-ethyl)fumaramido

Solvent system: 1% ethanol in chloroform

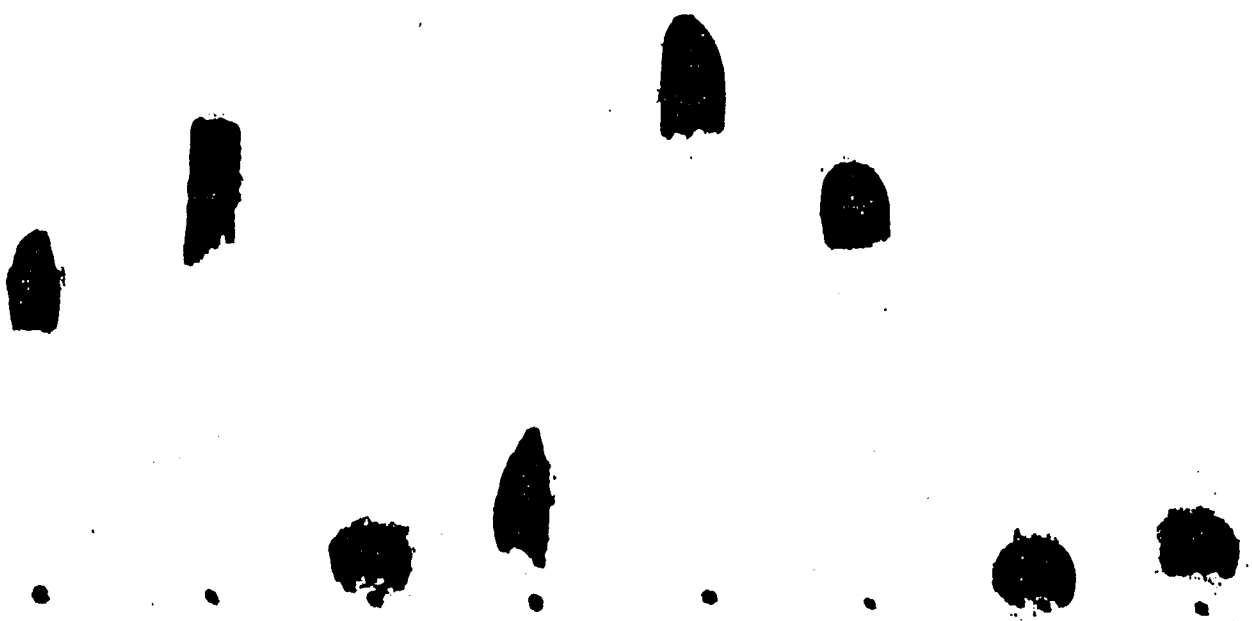


Ib: Benzyl 2-amino-4,6-O-benzylidene-2-deoxy-β-D-glucopyranoside

The remainder are derivatives of the above differing only at the 2 positon.

IIb: 2-formamido
IIIb: 2-(O-ethyl)oxamido
IVb: 2-(O-methyl)malonamido
Vb: 2-(O-ethyl)malonamido
IXb: 2-(1,2-diethoxycarbonyl)ethylamino
VIIIb: 2-(O-ethyl)malonamido
Xb: 2-(2-ethoxycarbonyl)ethylamino

Solvent system: 1% ethanol in chloroform



Ia IIa XIVa XXa Ib IIb XIVb XXb

Ia: Benzyl 2-amino-4,6-0-benzylidene-2-deoxy- α -D-glucopyranoside

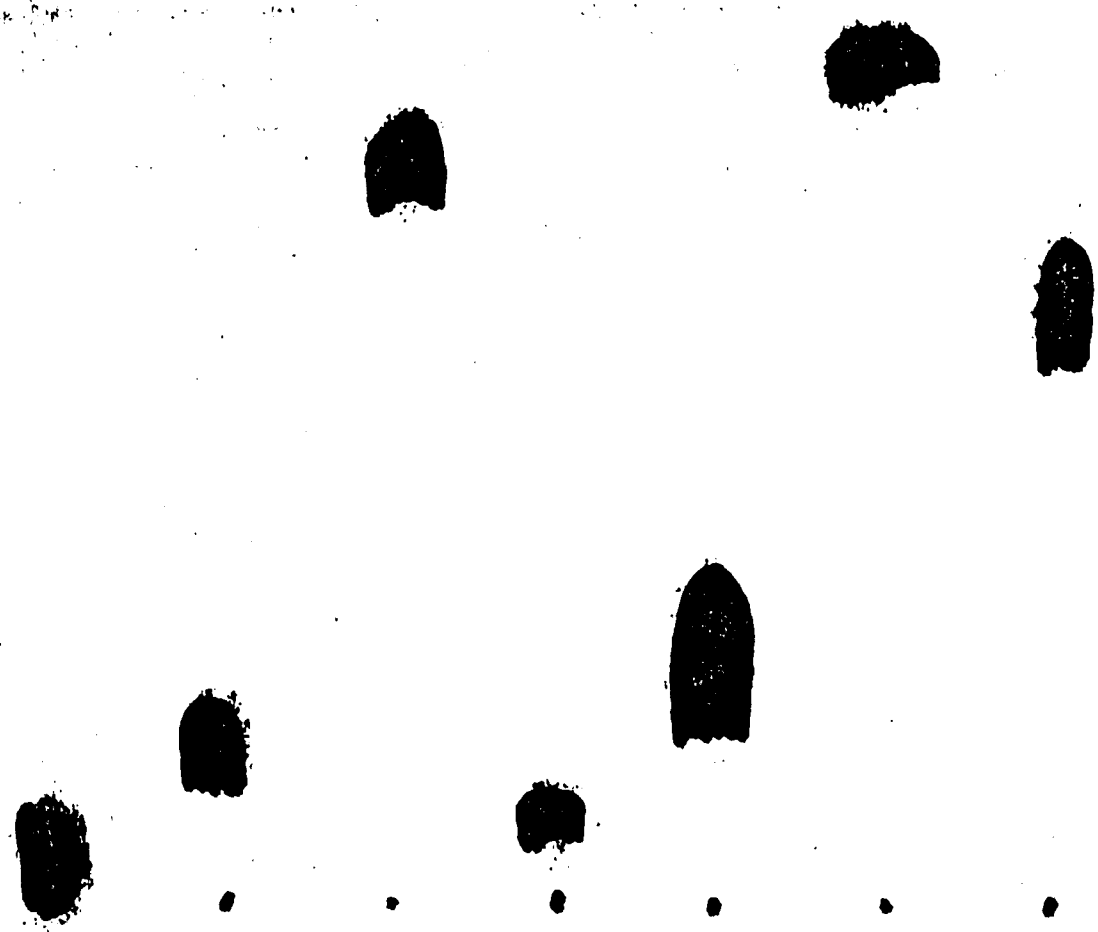
IIa: Benzyl 4,6-0-benzylidene-2-deoxy-formamido- α -D-glucopyranoside

XIVa: Benzyl 2-deoxy-2-formamido- α -D-glucopyranoside

XXa: Benzyl 2-deoxy-2-(0-ethyl)malonamido- α -D-glucopyranoside

Ib:
IIb: The β anomers of the above.
XIVb:
XXb:

Solvent system: 8% ethanol in chloroform



Ia XXVIa XXVIIa XXVIIIa XXXa XXXIa XXXIIa

Ia: Benzyl 2-amino-4,6-0-benzylidene-2-deoxy- ∝ -D-glucopyranoside

XXVIa: Benzyl 4,6-0-benzylidene-2-deoxy-2-(methoxycarbonyl) amino- ∝ -D-glucopyranoside

XXVIIa: Benzyl 4,6-0-benzylidene-2-deoxy-3-methoxycarbonyl-2-(methoxycarbonyl) amino- ∝ D-glucopyranoside

XXVIIIa: Benzyl 4,6-0-benzylidene-2-deoxy- ∝ -D-glucopyranosido-[2.3:4'.5'.] -2'-oxazolidone

XXXa: Same as XXVIa, only ethoxycarbonyl

XXXIa: Same as XXVIIa, only di-ethoxycarbonyl

XXXIIa: Same as XXVIIIa, only N-ethyl substituted

Solvent system: 15% petroleum ether in chloroform